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Björn Hausen

Woods Injurious to Human Health

A Manual

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A Manual

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Foreword

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Wood is a major article of commerce worldwide, its value and manifold uses are obvious but it is not generally appreaciated that wood and its products may be injurious to health. Operatives in the woodworking industries are the most seriously affected, by direct contact with wood, dust, and shavings, resulting in many cases of dermatitis and respiratory disorders, and they are also prone to contract more serious maladies such as cancer of the nasal mucosa, and Hodgkin's disease. A full understanding of these health hazards, leading to improved safety precautions, is clearly desirable.

The chemical constituents of wood are usually the causative agents, and in this book Dr. Hausen discusses both the chemical and medical aspects of these problems. A major part is devoted to a survey of the commercial timbers responsible for the development of contact dermatitis. The main culprits are simple quinones and catechols, which are subsequently oxidised to quinones, and a structure-activity relationship can be discerned.

Dr. Hausen has worked extensively in this area, and has identified several new quinones in woods known or alleged to produce allergic reactions on the skin, and confirmed their activitiy. In collecting all this information together in book form he has provided a valuable service to dermatologists, botanists, foresters, and organic chemists, and not least to those in charge in the woodworking industries.

Aberdeen, January 1981 R.H.Thomson

Preface

In response to the great interest expressed by many specialists from all over the world, this English edition of the German-language book originally published in 1973* has been made available.

As a result of the many research advances made since 1973 and the ever-increasing rate of import of tropical timbers among the various nations, this new edition has up dated and considerably enlarged. In order to provide rapid excess to desired information, the book contains a botanical index, a full subject index and an index of local, standard and trade names to help finding a way through the confused nomenclature of timber names. Of special interest to many readers will be the systematic review listing alphabetically all known wood species injurious to health.

Hamburg, January 1981 B.M.Hausen

* 'Holzarten mit gesundheitsschädigenden Inhaltsstoffen'. DRW-Verlag:Stuttgart 1973

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Furthermore I wish to thank all those who kindly translated the original articles to German or English: Mrs.Zeisske, University Library, Hamburg, Dr.Fumey, Togo, and Dr.Persch, Aulendorf for the translation from Russian (p. 70 and 90), Dr.K.Ito,Japan, for the translation of his own publications and other Japanese papers mentioned on page 131.

For the kindly supply of four *Diospyros* quinones, mentioned on page 85, I am most grateful to Dr.Sidhu, India, and for the mansonones, mentioned on page 91 I thank Prof.N.Tanaka, Japan. Finally I acknowledge the kindly supply of clinical pictures of patients allergic to tropical woods by Prof.K.H.Schulz, Hamburg and the patience of Mr.B.Schipke of the Photographic Division, Department of Dermatology of the University Hospital, Hamburg.

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I. Introduction

The use of wood for construction, furniture, veneer production, boat-building and many other purposes continues to increase; the production and export of wood for industrial uses has grown rapidly in recent years. The total world timber demand is about 2500 million m^3 per year, but nearly half of it is used as fuel (Figure 1). It is forecasted that by the year 2000 the demand will reach 4 - 5000 million m^3. Tropical rainforests, i.e. the Amazon basin, Central Africa, especially Zaire, and South-East Asia are the principal areas with substantial timber resources. Recent trends in the world timber trade show on one hand a large increase in tropical hardwood exports, especially from South-East Asia to Europe, and on the other hand an increase in the export of products of higher value from the primary producer countries, i.e. semi-finished and finished products. Nevertheless, the demand for such material as sawlogs remains the largest sector of tropical wood exports.
Of the group of main tropical hardwood producers - South-East Asia, West and Central Africa, South America - the smallest is Africa. Brazil, which is the largest producer in Latin America, only exports 2 % of its total output:

Producing area	Production in million m^3	Exports %(1974)
South-East Asia	55.82	60.42
West and Central Africa	11.79	56.31
South America	16.85	1.06

In the international trade of hardwood logs the tropical species play a dominant role; compared with Western Europe Japanese imports are striking: about 2 1/2 times that of the whole of Europe, 1/4 of its total consumption and ten times more than that of the United States:

	Japan	W-Europe
Imports compared with consumption	60 %	29 %
Percentage of total consumption	25 %	5 %
Usage in sawnwood and plywood	40 %	8 %
Usage in panel and paper manufacture	20 %	-
Proportion of roundwood in tropical hardwood import	95 %	>60 %

Tropical hardwood imports into West-Germany, France and Spain are nearly 60 %, in England log imports are less than 20 % of the total wood consumptions of these countries (Cibula 1980).
With the rising world demand of the industrialised countries and the increasing production of pretreated and semi-finished wood products in the developing countries, health problems are increasing in both due to contact with the dust and shavings that are created during the woodworking processes. Dust particles not only cause irritation of the mucous membranes of the nose, throat and eyes, and even effect inner regions

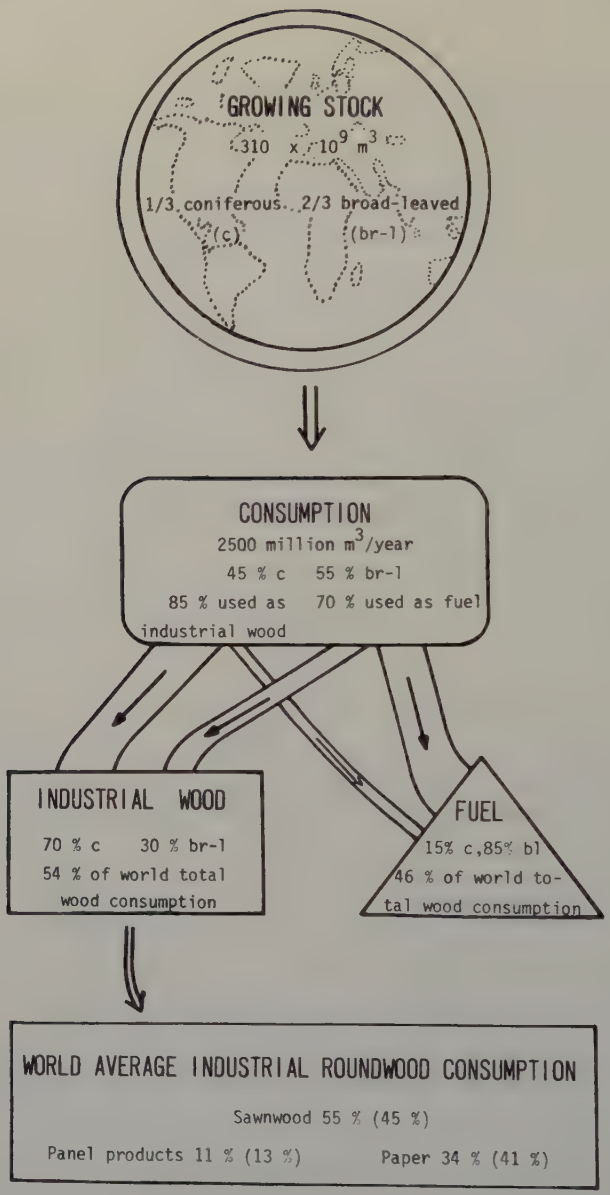
GROWING STOCK
310 x 10^9 m^3
1/3 coniferous (c)
2/3 broad-leaved (br-l)
CONSUMPTION
2500 million m^3/year
45 % c 55 % br-l
85 % used as industrial wood
70 % used as fuel
INDUSTRIAL WOOD
70 % c 30 % br-l
54 % of world total wood consumption
FUEL
15% c,85% bl
46 % of world total wood consumption
WORLD AVERAGE INDUSTRIAL ROUNDWOOD CONSUMPTION
Sawnwood 55 % (45 %)
Panel products 11 % (13 %)
Paper 34 % (41 %)

Figure 1 Main features of world wood consumption (in brackets: projections of the FAO for 1985) (modified from Cibula 1980)

of the respiratory tract, but also they frequently produce more or less severe lesions of the skin. Certain species produce general symptoms like headache, nausea,vomiting and cardiac arrthythmia, others damage the skin mechanically by bristles and splinters which is followed by infection. Last but not least cancer of the nasopharynx may develop in woodworkers, induced after several decades by steady contact with the fine wood dust. The affected persons are nearly almost employed in the woodworking industries as carpenters, cabinet makers, lumberjacks, sawmill operators, papermill workers etc. Those who enjoy working with wood as a hobby are rarely affected.

Most of the wood species described in the following chapters produce *allergic* reactions of the skin (contact dermatitis). The main problem a dermatologist is confronted with when consulted by a woodworker is *(allergic) contact dermatitis*; the information available being the visible skin reactions, the common trade name of the suspected wood species, and probably a sample of the wood dust or a piece of the timber. The patient probably noticed slight erythema of the skin and some itching months or years earlier while at work. At first recovery occurred during weekends, later on only on holidays. But one day the patient realised that his lesions were connected with his job and they became worse and worse. In this situation a decision had to be taken, either to consult a doctor or change his job. As a rule there is a delay of several years before medical advice is sought.

Provided that the woodworker shows relevant clinical skin lesions, knows the common trade name of the species, and presents a *piece*, not sawdust of the incriminated wood material it will be easy to clear the case. Exhaustive anamnesis (questioning concerning case history) will reduce the number of possible wood species and finally there remain not a hundred but only a few relevant eczematougeneous timbers which necessarily must be tested epicutaneously to discover the causative agents.
Finished articles or solid wood are seldom recognised as the source of contact dermatitis. In rare cases it may occur after prolonged contact with wooden bracelets, necklaces, knife-handles, wooden shoes (clogs) and musical instruments such as the mouthpieces of clarinets, flutes and recorders or the chinrest of a string instrument (see Rosewood). Jewellery made from Ebony, Brazilian and East-Indian rosewood and Olive wood has been observed to induce contact allergy in the wearer.

Thus we are not only faced with problems concerning the treatment of wood diseases but primarily with the prevention of their development which means that safety precautions must be devised to prevent contact with the dust, shavings, and in some cases even with the finished wooden product itself.

Reference

Cibula, E.J. Trends in timber supply and trade - an information review.
HMSO: London 1980

Incidence of allergic contact dermatitis and respiratory diseases caused by woods

The incidence of wood dermatitis, allergic rhinitis and bronchial asthma is not known. Similarly, no information is available on the incidence of wood poisoning. Compared with other trades the occupational risks from sawdust are probably not high. Some authors believe that most of the troubles connected with woodworking are due more to additives than to the wood itself (Bach 1980, Behrbohm 1957, Klaschka 1979, Stoke 1979). Only a few epidemiologically studies concerning the problem of wood dermatitis and respiratory disorders have been made in the last decade. The numbers given by Oleffe (1973,1975), Hublet (1972), Roman-Paris (1972) and Castagne (1976)from their native countries are not complete, because they cover only a small area or short period. However, the author is convinced that the problem is underestimated.

Seventeen to twenty wood species are held to be responsible for most of the troubles connected with wood dust contact and inhalation (Belli 1978, Bleumink 1973, Zafiropoulo 1968). It is noteworthy that certain timbers have such valuable properties that they are used despite their known toxicity and sensitising capacity, e.g. Mansonia, Pao ferro (Caviuna vermelha), Teak and Brazilian rosewood. Only in countries where allergic and in rare cases also toxic disorders must be reported to the *National Workmen's Compensation Bureau*, or the equivalent, are approximate numbers available every year. In Belgium(L'Office National de Sécurité sociale), France (Caisse de Sécurité sociale), West-Germany (Holz-Berufsgenossenschaft), Italy (Federazione Lavoratori delle Costruzioni), Switzerland (Swiss Accident Insurance Association) and other countries like Australia, Canada, England, the United States and the Soviet Unions the relevant organizations are required to publish - so far as the author knows - their statistical material in an annual report. However, in most annual reports cases of allergic contact dermatitis, rhinitis, bronchial asthma and poisoning are not separated from usual working accidents. In the United States each of the compensation laws is different in the fifty states and most give little attention to occupational diseases related with wood exposure. Thus it is very difficult to get reliable information.

Owing to the lack of such data from other countries, representative numbers are given here: from France 1968 and 1969 1 % (44/4124 - 1968; 40/4061 - 1969) and from West-Germany 63 reported cases of bronchial asthma and 227 cases of skin disorders in 1979 (Roman-Paris 1972, Holz-Berufsgenossenschaft 1979). Only one recent study from Switzerland gives such detailed information on injuries caused by woods that it is worth mentioning here (Hartmann 1978, 1980). In the period 1966 - 1978 165 cases were reported to the Swiss Accident Insurance Association (SUVA) of which 130 were allergic or non-allergic cases of contact dermatitis and 55 were respiratory disorders; there were 12 cases of classical bronchial asthma.

The following list is a selection of the reported cases and the responsible wood species; positive intradermal tests are given in brackets.

Botanical name	Trade name	s.l.	r.d.
*Chlorophora excelsa**	Iroko	34	4 (1)
*Mansonia altissima**	Mansonia	21	8 (1)
Dalbergia nigra; D.latifolia	Braz.; E-Indian rosewood	18	3
Tectona grandis	Teak	11	2 (1)
Terminalia superba	Limba	10 (?)	5
*Triplochiton scleroxylon**	Obeche	9 (?)	13 ! (5)
Pinus sylvestris	Fir	6	-
Picea excelsa, Abies alba	Spruce, Silver fir	6	-
Gossweilerodendron balsamiferum	Tola	6	-
Swietenia macrophylla	American mahogany	5	3 (1)
Fagus sylvatica	Beech	3 (?)	1
Tieghemella heckelii	Makoré	3	2
Bowdichia nitida	Sucupira	2	-
Gonystylus bancanus	Ramin	2 (?)	-
*Khaya anthotheca**	African mahogany	2	1
Juglans nigra	Walnut	2	2
Quercus robur	Oak	2	1 (1)
Sequioa sempervirens	Redwood	-	2
Cedrus libani	Liban cedar	-	2
Cordia goeldiana	Cordia	1	-

* Species also suspected by Oleffe et al. (1973,1975)

(?) Probably cases of contact urticaria ; s.l. = skin lesions, r.d. = respiratory disorders

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Clinical aspects

The action of wood on the human being may take place in the following different ways:

- mechanically, by splinters
- toxic, by shavings and dust particles that cause general symptoms after ingestion
- irritating, by dust particles which affect the skin and mucous membranes
- sensitising, by fine wood dust that produces allergic rhinitis, bronchial asthma, extrinsic allergic alveolitis (after inhalation) and allergic contact dermatitis by direct contact with the skin
- carcinogenic, by wood dust that causes adenocarcinoma of the nasopharynx

Mechanical irritation

Bristles and splinters may penetrate into the skin of persons handling the fresh cut timbers. Sometimes the wounds are slow to heal and complications arise from secondary infections (sepsis) when timber- or woodworkers have to labour under poor hygienic conditions. Woods which are blamed to cause such infections are Afrormosia, Douglas fir (Oregon pine), Greenheart, Limba, Mansonia and others containing toxic alkaloids or other poisonous constituents. Some wood species contain powdery material (often in the bark) which stains the skin or changes the colour of hair.

General symptoms

When pharmacologically active substances are absorbed through the skin, the respiratory tract or orally, systemic symptoms like headache, nausea, vomiting, giddiness, disturbance of vision, drowsiness, weakness, nosebleeding, salivation, thirst, loss of appetite, colic, muscular cramps and cardiac arrhythmia may occur. Pharmacologically active constituents such as alkaloids and glycosides are characteristic of Yew, Oleander, Mansonia, Afrormosia, Laburnum, and certain species of the Apocynaceae family, e.g. cytisine, N-methylcytisine and strychnine (Table 4, p. 25). The compounds may be absorbed from wooden containers, spoons, grill sticks, and spits. But these more extreme conditions of poisoning are rare (see Oleander, p. 95)

Mucosal irritation

Irritation of the nose and throat, difficulties in breathing, dryness and soreness of the throat, sneesing, as well as streaming eyes, nosebleeding, conjunctivitis and attacks of asthma are found in workers exposed to fine wood dust. The constituents of certain species produce sneesing during sawing which led to the name 'sneeze wood'. Examples are Kokko (*Albizzia lebbeck* Benth.) and Umtati (*Ptaeroxylon obliquum* (Thunb)

Radlk.). Generally, irritation of the upper respiratory tract is common, whereas real allergic rhinitis and bronchial asthma is rare. It has been described after prolonged exposure to Beech, Oak, and Western red cedar. Asthmatic attacks may be delayed for several hours after exposure to the sawdust. Symptoms belonging to the clinical picture of 'farmer's lung', also called 'extrinsic allergic alveolitis' or 'hypersensitivity pneumonitis' leading to a chronic damage of the lung tissue have been observed after exposure to the wood dust of Sequoia (sequoiosis) (Cohen 1967), Cork oak (suberosis) (Avila 1972) and others (see Chapter IV, p. 138). Sometimes they are caused by a fungus. This type of allergy is connected with coughing, dyspnoea, chill and fever (Arthus-phenomenon) developing 4 - 6 hours after exposure to the dust particles and is characterised by precipitating antibodies which can be demonstrated in the serum by the Ouchterlony-test.

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Primary irritant skin lesions

Primary irritation of the skin may be produced by the sap or latex which is typical of various species in certain plant families such as Apocynaceae, Euphorbiaceae, Moraceae and Anacardiaceae. Powders contained in the bark of trees, e.g. of Araroba, Tagayasan and Brigalow may produce rashes ('Brigalow itch') (Maiden 1912). Other wood species contain alkaloids with blistering properties, e.g. cryptopleurine in Poison walnut (p. 121) and chloroxylonine in East-Indian satinwood (p. 112), while sensitive areas of the body such as the corners of the mouth or the fingerwebs may become affected by quite mild irritants.

Strong sensitisers such as 3-(pentadec-8-enyl)-catechol from Poison ivy (*Rhus toxicodendron* L., Anacardiaceae) and primin from *Primula obconica* Hance (Primulaceae) include *both* types of biological activity at the same time: they are irritants *and* sensitisers. In *high* concentrations, for example at 1 %, their effect is a primary irritation, in *low* concentrations, e.g. 0,01 % they only elicit a reaction in a sensitised person (or animal). Wood dust and shavings containing an *unknown high* amount of a sensitiser thus will affect *every* worker by causing erythema, vesicles, blisters and even bullae. Therefore a patch test with the actual wood dust may produce *false positive* reactions (see Diagnosis of contact sensitivity, p. 14) and is difficult to interpret if it is not followed by sufficient controls.

Reference Maiden, J.H.: Agric.Gaz.New South Wales **32**, 206 (1921)

Contact urticaria

Contact urticaria is a weal and flare reaction of the skin elicited by cutaneous contact with wood shavings or with the wood itself. Though non-immunological types of reac-

tions may be produced by some species immediate reactions based on immunological mechanisms are more characteristic. Species which have induced such reactions include Obeche, Larch, Limba, and occasionally Teak (Schmidt 1978). A state of acute sensitivity is proved by rubbing the patients skin - moistened slightly before by water - with a piece of the suspected wood species 20 - 30 times on the forearm according to the 'rubbing test' of Oehling (1963) and Gronemeyer (1967). By this proceeding urticarial reactions are produced within several minutes yielding a large weal and flares while the non-offending species remain ineffectual. To the same extent no reactions will be seen with the offending wood in controls.

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Oehling, A.: Allergie Asthma **9**, 312 (1963)
Schmidt, H.: Contact Derm. **4**, 176 (1978)

Allergic contact dermatitis

Several defence mechanisms enable the human skin to protect itself against injuries. Where this protection is overcome rash, inflammation, dermatitis (eczema) and damage is produced accompanied by itching and followed by pustules, vesicles, blisters, ulcers and necrosis. Maintained contact of the skin with sensitisers smoothes the way for specific hypersensitivity. However, prolonged predamage of the skin by frequent contact with acids, alkali, detergents, disinfectants, hand cleansers, solvents, thinners or generally wet working conditions, facilitates penetration into the skin and hence sensitisation. In some cases the usual slightly acid conditions of the normal human skin (mainly pH 6 - 5, in some cases pH 6,8 - 4) facilitates the 'extraction' of certain constituents from the dust particles, shavings or the wood itself. Sweat conditions, even more acidic initially (ca. pH 4,5) and varying between 4,5 and 8,4 in most healthy people may intensify this process. Generally dermatitis affects those who are working with the wood for a long time. Under occupational conditions an extremely close contact occurs between wood dust and the skin. Thus, the first clinical symptoms appear at the exposed sites, i.e. the back of the hands, the forearms and the eyelids. Later on the lesions spread out to the face and neck (Figure 2, a - c) and finally the whole body becomes involved. Fine dust particles settling on the skin and clothes are manually carried to the genitals, become trapped between the clothes and skin, especially at the neck and sleeves and occasionally involve the legs by entering from the bottom of the trousers. Wood dust particles also attain to the sweaty body areas such as the axillae and groins, in severe cases to the ankles, waist and dorsa of the feet. The acid conditions of sweaty regions in combination with the enzymatic activities of the skin result in oxidation of harmless wood constituents to efficient allergens. Examples are phenolic substances which may be oxidised to sensitising quinones in the skin.

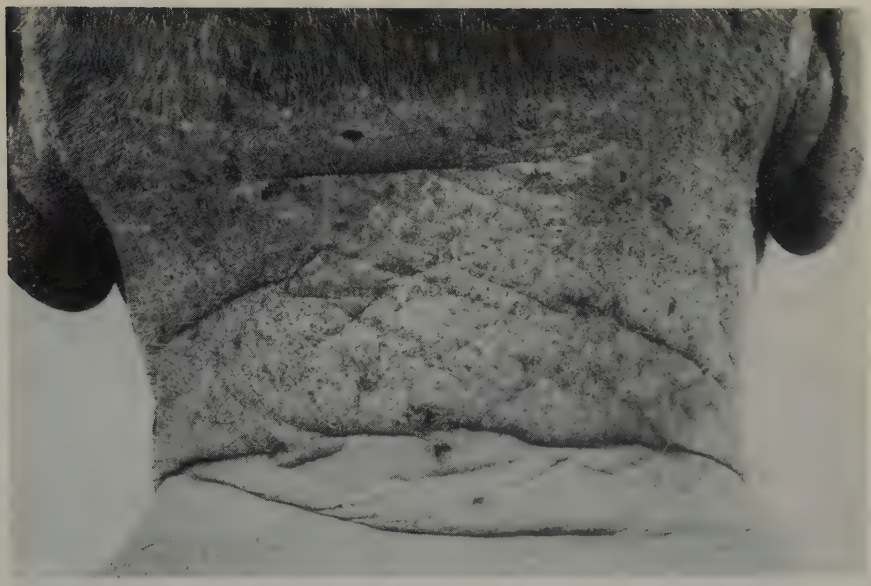


Figure 2 a,b
Allergic contact dermatitis of the face (right) and neck (above) due to sensitisation by an exotic wood species (Teak)

Figure 2 c Allergic eczematous reactions of the hands and forearms

The clinical symptoms start with mild reactions consisting of itching erythema and burning sensitisation of the unprotected body areas. In the due course papules, vesicles and exudation appear; with time the involved skin becomes thickened and fissured followed by lichenification. Due to recurrent contact the individual develops an allergic condition, i.e. the woodworker becomes sensitised to the wood constituents. The latent period extending between the first contact with a wood species and the development of the first visible allergic reactions varies from a few weeks to several years, the shortest time being seven days (see Immunological aspects). Every renewed contact with the sensitiser produces a stronger outbreak of dermatitis; the attacks become more frequent and lesions increase in severity. In serious cases the work must stop. All clinical symptoms subside within a short time when the patient is removed from his place of working, for example during holidays, occasionally already at weekends.

Immunological aspects of allergic contact dermatitis

During work with wood species the epidermis is continuously exposed to a wide variety of potentially sensitising constituents, which are simple chemical haptens. Thus

contact allergy expressed on the skin as contact dermatitis is caused usually by substances of low molecular weight varying from 150 to 1000. In contrast to the mainly high molecular weight antigens of immediate type allergy (type I, anaphylactic reactions) and extrinsic allergic alveolitis (type III, Arthus phenomenon) (Gell & Coombs, 1967) which are mostly unknown the structure of the low molecular weight contact allergen in wood species is known or easily determined.

According to the generally accepted definition *allergy* is understood today as
a specifically acquired, altered capacity of the body to react to foreign substances based on a pathological antigen-antibody reaction (type I to III)
and/or
a pathological reaction due to specifically sensitised T lymphocytes
(type IV, cell-mediated type of allergy, delayed type) (Gell & Coombs).

As most of the allergic diseases caused by exotic wood species belong to the delayed type, recent approaches to the understanding of immunological proceedings occurring during induction of cell-mediated hypersensitivity (allergic contact dermatitis) will be discussed here briefly.
Generally sensitisation will develop in a person when this individual is genetically predisposed towards an allergy and/or the following basic requirements are fulfilled:
a more or less *high sensitising poteney* of the agent
attachment of *sufficient amounts* of the allergen to the skin
suitable *intensity of action* of the compound on the skin.

More than 90 % of the low molecular weight allergens reaching the skin during contact with the wood or dust are either repelled by the horny layer or escape from the application site by direct penetration through the epidermis and dermis without being bound (the 'wrong way'). Only small amounts are actually retained and effectively induce sensitisation. These small amounts are picked up by the Langerhans cells (LCs) and their dendrites localised in the epidermis below the Stratum corneum (Figure 3). The suprabasal location of the LCs within the epidermis plays a sentinel (protective) role by equipping the cutaneous surface (skin) with an elaborate network of interlocking dendrites just beneath the keratinised layer, prepared to capture foreign material. The strategically important point delegates the LCs to the most peripheral outpost in the afferent limb of the immune response, i.e. the Langerhans cells form a reticulo-epithelial trap for external contact allergens.
Low molecular weight compounds applied to the skin are first bound to the Langerhans cells and then presented in association with HLA-D/DR antigens (surface antigens of LCs and macrophages) to the T lymphocytes. These HLA antigens (human leukocyte antigen gene products) are encoded for by the D/DR region of the 6. chromosome and are expressed on the surface of stimulator cells - such as Langerhans cells and macrophages . Binding of the hapten modifies them to a 'hapten-surface antigen complex'.

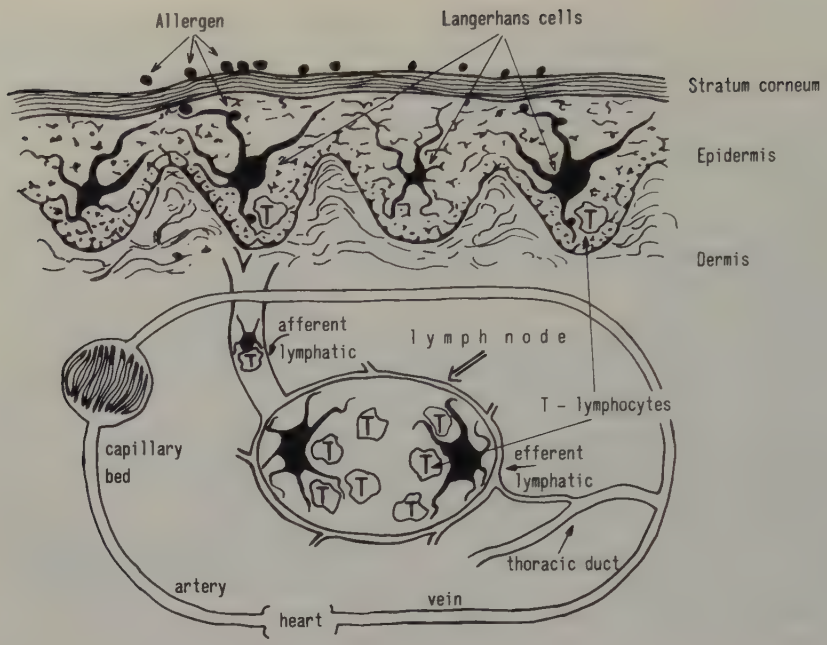


Figure 3 Pathway of external low molecular weight allergens during induction of contact sensitisation

When the hapten-D/DR complex is presented to the epidermal T lymphocytes the presented structure is recognised as 'altered self'.

Close apposition of mononuclear cells (T lymphocytes) to Langerhans cells is frequently seen in the epidermis and dermis within three hours after elicitation (application of the allergen to prove the induced sensitivity). After four to six hours increased numbers of LCs, most of them apposed to T cells, enter dermal lymphatics and circulate to the regional lymph nodes. The LCs in apposition to lymphocytes gather in the cortices of the lymph nodes. It is supposed that the LCs present the foreign substances (allergens) to T lymphocytes in the epidermis and dermis as well as during migration to dermal vessels and the draining lymph nodes. The role of LCs as antigen-bearing and presenting cells in the epidermis is adopted in the *dermis* by the macrophages.

In the paracortical region of the draining lymph nodes the stimulated small T lymphocytes proliferate and are transformed into immunoblasts which further differentiate into two subpopulations of specifically sensitised small lymphocytes: the *effector cells* and the *memory cells* . The *memory cells* recirculate between the thymus-dependent areas of the lymph nodes (paracortical region), the spleen, and the ductus thoracicus storing the information of previous contact with the initial allergen.

Upon a new contact with the sensitising substance they are able to proliferate and differentiate into a new progeny of sensitised small lymphocytes (effector and memory cells). The other subpopulation of sensitised T lymphocytes, the *effector cells*, circulate in the blood and thus return to the skin where they react with the residual of the applied allergen (hapten-D/DR complex on the surface of the LCs) which sometimes results in a flare-up phenomenon recognised on the seventh day after the first application or they react to a new exposure with the specific allergen by releasing soluble substances, so-called lymphokines, which initiate the inflammatory skin reactions.

Selective uptake of allergens by LCs as well as interactions between Langerhans cells and T cells in the epidermis respectively between macrophages and T lymphocytes in the dermis are restricted genetically by the HLA system. The D/DR genes of the HLA chromosomal complex control the cell surface markers which are only present on the stimulator cells, i.e. Langerhans cells in the epidermis and macrophages in the dermis. Effective Langerhans cell - T cell respectively macrophage - T cell interactions are only possible when the stimulator cells and the responder lymphocytes are syngeneic. By taking up the antigenic material the syngeneic surface D/DR antigen of the LC is changed to 'altered self'. This event finally induces the specific cell stimulation, proliferation and differentiation for which close physical cell to cell contact is required.

In conclusion: the major mechanism of induction of contact allergy is a direct conjugation of the sensitising substance to D/DR surface antigens of the Langerhans cells located in the epidermis and/or the D/DR gene products of the macrophages in the dermis (the 'right way'). In contrast, exposure to a contact allergen via the intravenous route (injection), via ingestion or by penetration through the epidermis and dermis directly into the general circulation without binding to the surface antigen of the LC or macrophage - but probably to another cell particle, erythrocyte, protein etc.- which happens when supraoptimal amounts of the allergen are applied to the skin - most of which cannot be conjugated to the LC D/DR antigens ('wrong way') - will result in tolerance instead. It is important to state that sensitisation only takes place when the 'right way' is followed, i.e. appropiate presentation of the allergen by LCs to T lymphocytes.

When Langerhans cells are absent from the skin, e.g. by prolonged exposure to UV light, or are significantly altered in their physiological properties, the sentinel network is breached and a completely different immune response results: Exposure to external allergens (even other foreign agents such as, for example, virus-antigens) not only fail to sensitise, respectively are not presented, but evoke profound and specific immunological unresponsiveness.

References

Gell, P.G.H. & Coombs, R.R.A.: Clinical aspects of immunology. Blackwell Sci. Publ: Oxford, 1967

Diagnosis of contact sensitivity

Usually patch tests are performed on the back of the patient. The patches are applied in five units taped on the upper back in vertical rows. The plasters are left on for 24 hours. Readings are carried out after 24, 48 and 72 hours. The patch test site should be marked accurately, otherwise identification of positive reactions becomes difficult or impossible. In normal practice fine wood dust particles or shavings are applied, but extracts of the wood in *subtoxic* doses or the pure sensitiser (if available) in a non-primary irritant concentration are preferable. Though only two of the known sensitising wood constituents (juglone, thymoquinone) are commercially available (as far as the author knows) as yet, the correct concentrations of the more important ones are listed in Table 1.

An allergic reaction will develop when the correct concentration of an allergen or wood extract is applied to the skin of a sensitised person. This concentration will give no reaction in controls.

In all cases of positive reactions to wood dust particles, shavings or wood extracts it is necessary to clear up whether the test response is really an allergic one or not, as *false positive reactions* (non-allergic positive; primary irritant) may occur due to the fact that an allergic reaction may differ very little from that producing an irritant response.

If there is any doubt adequate controls in at least 20 people (Cronin recommends 50 controls) are essential. For example a *false positive reaction* is obtained when the concentration of the sensitising substance in the sawdust or extract is too high. Thus, if there exists any such possibility the primary irritant threshold of the crude wood extract should be ascertained *before* patch tests are performed on the skin of the sensitised patient. (Experiments on guinea pigs are more preferable).
Another possibility for determining the correct concentration is to apply an initial test with lower concentration, for example 0,1 to 1 %. If the result is negative, the concentration may be increased stepwise.
However, *false negative reactions* (missed allergic positive) may also occur when the concentration of the sensitiser in the wood or its crude extract is too low to elicit a skin response, or when corticosteroid-containing medicaments suppress the reaction. In the first case it may help to test another sample from another source, but it is important to remember that the *same offending species* must be chosen. In the second case four to five days should elapse before the test is repeated (in the case of a corticosteroid injection four weeks must elapse).

It is known that results are frequently misinterpreted, however, the general rule is that allergic reactions are reproducible, but irritant responses stop abruptly when testing is performed with subsequent dilutions.

Table 1 Concentrations of essential contact allergens of wood species for epicutaneous tests

Sensitiser	Timber	Concentration %
Anthothecol	*Khaya anthotheca* C.DC	1
Chlorophorin	*Chlorophora excelsa* Benth. & Hook.	1 - 10
Cordiachromes	*Cordia* and *Patagonula* species	0,1
Deoxylapachol	*Tectona grandis* L.; *Tabebuia sp.*	0,01 - 0,1
R-3,4-dimethoxydalbergione	*Machaerium* species	0,01
S-4,4'-dimethoxydalbergione	*Dalbergia* species	1
S-4'-hydroxy-4-methoxydal.	*Dalbergia* species	1
2,6-dimethoxy-1,4-benzoquinone	various wood species	10
Lapachol	*Tectona grandis* L.; Bignoniaceae sp.	1 - 10
'Macassar quinone'	oxidation product of macassar II from *Diospyros celebica* Bakh.	1
Mansonone A	*Mansonia altissima* A.Chev.	0,1
Obtusaquinone	*Dalbergia retusa* Hemsl.	1
Oxyayanin A and B	*Distemonanthus benthamianus* Baill.	1
Thymoquinone	*Calocedrus decurrens* (Torr.) Florin	0,1

The intensity of the skin reactions after patch testing is evaluated according to the following scale, generally accepted by most of the dermatological clinics in Europe. But in contrast to the English and Amaerican interpretation of +? and ± which means a doubtful reaction, (+) is recorded in this book as a distinct weak reaction.

		Score
∅	no reaction (negative)	0
(+)	slight spotted erythema	0,5
+	distinct erythema restricted to the test area	1
++	distinct confluent erythema and infiltration, slight swelling	2
+++	intense erythema, infiltration and exudation with swelling and spreading out over the test area	3
IR	irritant	
NT	not tested	

Active sensitisation may occur, e.g. in controls when the concentration of the test substance is too high and the compound is a strong sensitiser.

Characteristics are

- flare-up phenomenon: positive test reaction at the test site 10 - 14 days after application
- positive test reaction in a non-sensitised control after restesting some days or weeks or months later.

Examples have been observed with Pao ferro allergen (*Machaerium scleroxylum* Tul.) which is the strong sensitiser R-3,4-dimethoxydalbergione and with deoxylapachol from Teak.

Extracts of wood dust or shavings are easily obtained by leaving 1 g of the wood particles with 9 ml ethanol overnight (or longer) at room temperature. After decanting or filtration a 10 % stock solution is obtained which may serve for test purposes after subsequent dilution. As ethanolic extracts are not stable over a longer period because the solvent tends to evaporate and thus to concentrate the extract incorporation into and storage in petrolatum (vaseline) is a suitable base for allergen preservation.

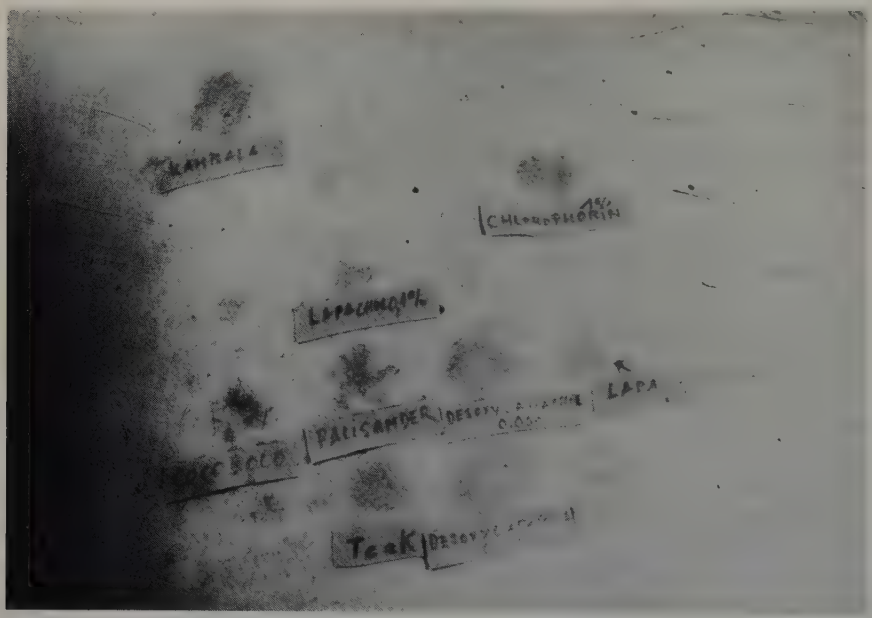


Figure 4 Positive allergic skin reactions after patch testing with different wood extracts and pure sensitisers
Explanation: Kambala (*Chlorophora excelsa*); sensitiser: chlorophorin
Palisander = Brazilian rosewood (*Dalbergia nigra*); Cocobolo (*Dalb. retusa*)
Teak (*Tectona grandis*), sensitiser: deoxylapachol, eliciter: lapachol;
Lapachonon = lapachenole (*Paratecoma peroba*), probably a cross-reaction

Preparation of stable wood extracts have been successfully achieved in our laboratory by evaporating the extract to dryness, mixing the residual material with white petrolatum (1 + 9) for at least a half hour to get a homogenous paste which then is transferred to 1 ml syringes and stored in the refrigirator. Protection from light is ensured by covering the syringe with aluminium foil. From our experience extracts prepared in such a manner and diluted to non-primary irritant concentrations may be stored for years without losing their allergenic potency. Even relatively unstable wood constituents such as deoxylapachol have been stored for more than one year.
Positive test reactions are shown in Figure 4.

References

Cronin, E. Contact dermatitis. Churchill Livingstone: London, 1980

Botanical identification

Correct identification of the offending wood species is absolutely necessary, otherwise any patch test is meaningless. Trade names are not only often misleading, but in most cases insufficient and confusing. Often one single name is used for a large number of different timbers, for example 'rosewood' for 30 different wood species.
On the other hand, for one definite species more than ten different trade names may be in use. An example is *Chlorophora excelsa* Benth. & Hook. which is called Iroko, Kambala, Sanga-sanga, Teak, Odum, Mvule, Mvalo, Tule, Intule and Moreira etc.
Tree nomenclature sometimes originates from native designations, and occasionally derives from the harbour from where the timbers are shipped; sometimes they are based on their colour or the names may be pure fantasy. However, one thing they all have in common: incorrect names are misleading and the source of severe mistakes, occasionally leading to serious commercial losses. Timbers shipped under false name to certain destinations may be damaged by natural forces, because their physical properties essential for construction do not correspond to the required quality of the original species. In many cases skin lesions are caused in woodworkers because the species in use is not the original, but a substitute with irritating and sensitising properties (see Pao ferro). Therefore in any case of skin diseases, health injuries or allergic reactions of the respiratory tract connected with imported wood, a solid wood sample - not wood dust - should be sent to an expert (*wood anatomist*), with a note of its origin and available trade names for specific botanical identification.
A patch test in a suspected allergic patient is only valuable with a satisfactorily identified wood species. Later re-examination of the patient's allergic condition in the case of a recurrence, and chemical investigation of the offending wood are impossible when the original wood sample is not available and the patient can only remember 'rosewood' for the incriminated species. A voucher sample should be kept at all events! The confused nomenclature has caused such trouble that a lot of earlier reports are completely unreliable (see also Index on page 182).

Protective and precautionary measures

Increased use of exotic timbers reinforces the problems of prevention and treatment of allergic diseases. Generally safety precautions may be realised by removing the offending hazard or protecting the workmen from any possible contact with the wood dust.

Dust extraction by exhaust ventilation for moulders, sanders, polishers, circular saws, and other machines and working places are the most important precautionary measures. Occasionally moistening of the air with water or oil at the point where wood dust is generated may be successful.

Under normal conditions protection of the woodworker includes

- Protective clothing with long sleeves, a high collar, gauntlets (rubber gloves) and - if necessary - masks against irritating and sensitising dust particles
- Barrier creams, silicon-free and fatty, to be used before,during and after working. The idea of a barrier cream is to prevent deleterious substances reaching the skin and to operate as a so-called 'invisible glove' with the aim of limiting the incidence of dermatitis. Though some barrier creams are efficient, most of them fail in practice to prevent the development of dermatitis, because the layer is too thin or they could not be washed off, even with strong cleansers. Thus considerable scepticism about the value of barrier creams still exists and much further investigation remains to be done in this field, preferably under working conditions, before the effiency of barrier creams reaches the degree of protection required in the wood working industries
- Adequate washing facilities including showers
- Education of the woodworkers regarding care in handling and the avoiding of indue exposure to dusts which are known to possess irritant and sensitising properties. In particular workers should be discourages from using petrol, turpentine, thinners, organic solvents, and harsh soaps to remove the day's grime, as these materials may damage the skin by primary irritation and enhance the penetration of eczematous compounds thus paving the way for subsequent sensitisation
- Workers should be selected individually before being assigned to a definite job in order to avoid that workmen are engaged at a working place who belong to the atopics. Such workers should be kept under close observation and removed from work if any eruption occurs
- Some authors mention that nasal sprays with antihistamines have been found to be useful in some cases against the irritating dust of certain wood species.

Early and correct diagnosis of an occupational outbreak of allergic contact dermatitis is of great importance. If the causative wood species is easily recognised and identified, removal from the factory or protection of those sensitive to it is essential to prevent disability. However, if it is a valuable species with no adequate substitute its continued use should be allowed but with greater insistence on dust control, protective clothing and similar protective measures. These measures are likewise valid for any other wood dusts with poisonous or hazardous properties.

In rare cases replacement of the sensitising species by a less sensitising but effective alternative may be possible. It is worth mentioning that replacement sometimes means replacement of a whole consignment of an offending timber by the same species from another locality, e.g. of irritating and sensitising Teak from South-East Asia by an allergen-free Teak grown in Africa.
It is generally known that considerable differences in the amount of allergenic and irritating constituents may occur in timbers. Thus a preliminary chemical investigation of the imported wood before the whole consignment is accepted or transported to the consumer sometimes may prevent workmen's disability and commercial losses.
From our experience the allergen content in the same species from different localities may vary considerably; for example some years ago an inspection revealed that out of four specimens of Mansonia (*Mansonia altissima* A.Chev.) from different yards in Hamburg (West-Germany) only one contained enough of the allergenic mansonone A to induce allergic sensitisation as well as eliciting allergic reactions in presensitised individuals. Similar experience has been gained with Teak.
No protection exists against the accidental appearance of an irritant timber as an erroneous sample in a normal shipment other than that just mentioned.

Once a sensitisation has established topical application of corticosteroid ointments is indicated. Though several efficient topical steroids are available, a long treatment is not recommended. Any dermatologist confronted with outbreaks of dermatitis in a factory knows that recurrent dermatitis is only countered efficiently by *strict avoidance* of further contact with the offending wood species.

Sensitised patients should be given employment in some other capacity (of the same plant - if possible) to protect them from further contact with the sensitising wood and cross-reactive species.

When contact allergy has been manifested so strongly that work has to stop a report to the National Workmen's Compensation Bureau (or the equivalent) is necessary which in most European countries and abroad will pay for retraining and/or accept responsibility for the costs of an appropriate annuity.

Retraining should not involve occupations that bear the renewed risk of recurrent allergic reactions. Possibilities of cross-reactions to chemically related compounds in another working place exist in individuals that are sensitive to certain quinonoid wood constituents - such as deoxylapachol, lapachenole, mansonones, dalbergiones etc.- and change their job to that of a gardener, florist or pharmacist. In this case contact may occur with related quinones - such as primin, cypripedin etc.- occurring in flowers and drugs derived from other plant families, as shown in Figure 5.

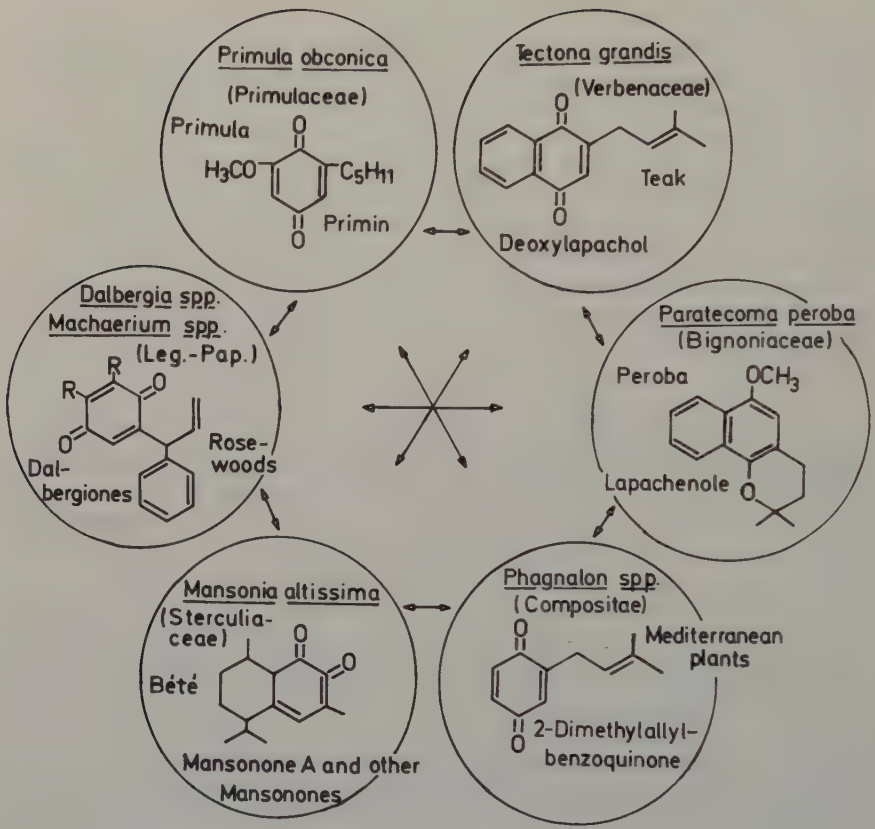


Figure 5 Cross-reactions obtained experimentally in sensitised guinea pigs between quinonoid constituents of plants and woods

Wood chemistry

The toxic, irritant and sensitising constituents of woods are 'accessory' substances which mainly occur in the heartwood. Most of them are extractable by organic solvents. Often they have a function as protective agents against injury or attacks by fungi, insects (termites) and bacteria. Most of them must be considered as by-products and end-products of the biological functions of a living tree, which are of no further use for the species and therefore are stored in the dead cells of the heartwood, colouring it differently.
Bark and sapwood may contain constituents differing from those of the heartwood or they may be the same ones but in differing amounts. It is a general observation that wood dermatitis is mainly caused by the heartwood constituents of tropical species. The amounts of the responsible sensitisers vary seasonally, geographically and even between specimens growing in the same place. Sometimes trees located only 3-4 m from one another contain ten fold differing amounts of the same constituent.

The more rare cases of contact dermatitis in wood cutters debarking trees and local timber workers are mostly due to the compounds of the outer sapwood and lichens growing on the bark. Occupational dermatitis among forest workers, called 'wood cutter's disease' is caused by contact with lichens, liverworts and mosses of the genera *Cladonia* (mainly *C. alpestris* L.), *Parmelia, Usnea, Frullania (F. tamariscii, F. dilatata, F. nisqualensis*) and *Isothecium*. Though usnic acid and atranorin have been incriminated as the causative agents, the allergens of most cases of 'wood cutter's disease' are sesquiterpene lactones such as frullanolide (see Beech). In *Frullania*-sensitive patients cross-reactions to Compositae species such as *Chrysanthemum* and *Taraxacum* (dandelion) have been observed.

The botanical families containing species with toxic and/or sensitising properties are well known. Those including only sensitising species are listed in Table 2.

Table 2 Botanical families containing species with sensitising properties (mainly timbers; the Anacardiaceae include shrubs)

Family	Number of species
Leguminosae	109
Anacardiaceae	32
Meliaceae	27
Bignoniaceae	21
Lauraceae	18
Cupressaceae	13
Ebenaceae	13
Pinaceae	13
Moraceae	12
Boraginaceae	7

Family	Number of species
Sterculiaceae	7
Sapotaceae	6
Menispermaceae	6
Proteaceae	3
Verbenaceae	2
Burseraceae	1
Oleaceae	1

The wood constituents responsible for injuries to human health belong to different chemical classes and possess different physiological or pharmacological properties. Table 3 reviews the types of compounds which alltogether have been found harming human beings. Apart from the quinones all other classes are only little involved.

Table 3 Wood constituents and their effects

Type of compound	Effects
Alkaloids	toxic, sometimes histamine-liberating
Anthraquinones	primary irritant, especially when ingested, rarely sensitising
Benzo- and naphtho-quinones	sensitising, in high concentrations primary irritant
Catechols	strong sensitisers, primary irritants
Flavonoids	cardiac effects, increase of blood pressure, purgative, seldom sensitising
Furocoumarins	phototoxic, seldom sensitising
Glycosides	mainly cardiac effects
Minerals	primary irritant by mechanical action
Phenols	primary irritant, sensitising
Saponins	haemolytic, irritant
Sesquiterpene lactones	sensitising, also irritant
Stilbenes	sensitising, also irritant (suspected to be carcinogenic)
Terpenes	sensitising, also irritant

While toxic reactions, systemic effects and cardiac symptoms are mainly caused by alkaloids, flavonoids and glycosides, the principal allergens of which most are primary irritants in high concentrations, are benzo- and naphthoquinones and phenolic compounds (including the catechols). The latter are easily oxidised to the corresponding quinones in the skin.

Sensitising catechols, which are the most potent sensitisers from natural sources, are mainly found in the Anacardiaceae family, e.g. in Poison ivy (*Rhus toxicodendron* L.), Poison oak (*Rhus radicans* L.), Japanese lacquer tree (*Rhus vernicifera* DC) and are well known in the family of Proteaceae and Ginkgoaceae.

During penetration into the skin the catechols are enzymically oxidised to the corresponding pentadecyl-quinones. However, as source of occupational contact allergy in woodworkers their role is relatively minor due to the fact that only a few members of these families, e.g. Espavel (*Anacardium excelsum* Skeels), Gonçalo alves (*Astronium fraxinifolium* Schott), Quebracho (*Schinopsis balansae* Engl.) and Dao (=Paldao)(*Dracontomelum dao* Merrill & Rolfe) are timbers of commercial value.

The occurrence of allergy-inducing quinones is not restricted to one or two families but widely distributed among Bignoniaceae, Boraginaceae, Ebenaceae, Leguminosae etc. The results of recent investigations and clinical observations have revealed that quinones are increasingly important etiological agents responsible for occupational woodworker's dermatitis.

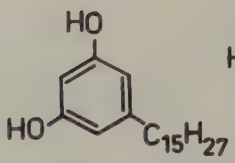
Examples of toxic, irritant and sensitising wood constituents not further mentioned in the following chapters and the **Systematic review** are given in Table 4.

Returning to the *Immunological aspects* it must be remembered that evidence is accumulating that stimulator cells such as Langerhans cells in the epidermis and macrophages in the dermis play the most important role in allergic contact allergy. It is undoubtedly clear that the bound foreign substance - the low molecular weight allergen- is presented to the immune competent cell - the T lymphocyte - during cell-to-cell apposition and that the presented 'hapten-surface antigen complex' is recognised as 'altered-self'.

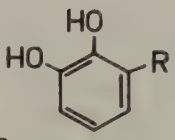
Binding of the contact allergen to the D/DR surface antigen of the Langerhans cells is the basic presupposition for the induction of an allergy of the delayed type. The conjugation takes place more easily the more reactive the captured compound is. Quinones are highly reactive chemical substances. Nucleophilic attack on unsubstituted carbon atoms of the quinone ring in benzo- and naphthoquinones occurs with SH- and NH_2-groups of the amino acids forming the histocompatibility antigens of the Langerhans cells and macrophages (D/DR antigens).

Based on this understanding it is obvious that only those benzo- and naphthoquinones having at least one free quinone position may function as primary sensitisers (inductors). When all positions are blocked by substituents conjugation to the cell surface antigens is inhibited or nearly impossible.

Clinical observations and results from animal experiments with known plant and wood benzoquinones have demonstrated that preferred sites of nucleophilic attack on benzoquinone rings are positions 3 and 5, dependent on the character of the functional groups in positions 2 and 6. For example in primin, where the group in C-6 is a methoxy-group and the chain at C-2 is n-pentyl (C_5H_{11}), position 5 is more electrophilic (while position 3 is hindered by the C_5H_{11}-group) than for example in a compound with a hydroxy-group at this site (drawing on page 26).

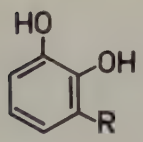


Cardol

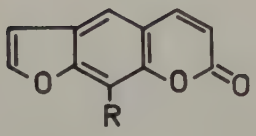


Renghol R = $C_{15}H_{29}$
Laccol R = $C_{17}H_{31}$
Glutarenghol R = $C_{17}H_{33}$

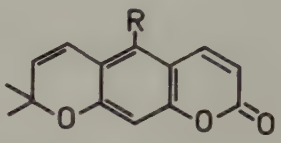
Catechols in Anacardiaceae :



R = $C_{15}H_{27}$ and R = $C_{17}H_{28}$; 8,11,13 and 8,11,14 trienyl side chains in Poison ivy and Poison oak
Rhus toxicodendron L., R.vernicifera DC, R.radicans L. and R.diversiloba TORR. et A.GRAY

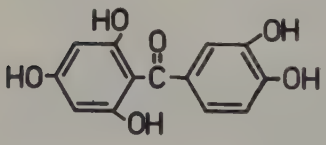


Coumarins
(Rutaceae)



Psoralene (R = H)
8-Methylpsoralene (R = CH_3)
Xanthotoxin (R = OCH_3)

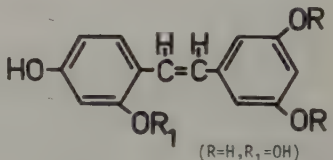
Xanthyletin (R = H)
Xanthoxyletin (R = OCH_3)



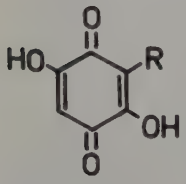
Maclurin

Maclura pomifera RAF. (Osage orange)
Chlorophora tinctoria GAUD. (Fustic)

Stilbenes
(Moraceae)

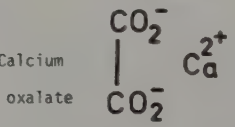


(R=H,R_1=OH)
2,3',4,5'-Tetrahydroxystilbene
Pterostilbene (R = CH_3, R_1 = H)



Rapanone R = $C_{13}H_{27}$
Embelin R = $C_{11}H_{23}$
Ardisia macrocarpa WALL.
Rapanea maximowiczii KOIDZ.
(Myrsinaceae)

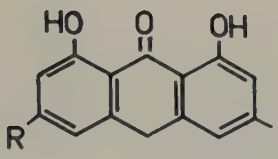
Quinones



Calcium oxalate

Mineral
(in various wood species)

Table 4 Chemical structures of toxic, irritant and sensitising wood constituents not repeated in the following chapters



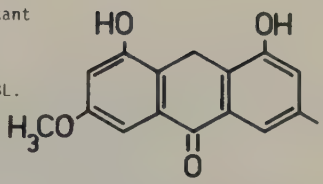
Skin and mucosa irritant

Anthrones

Vateirea guianensis AUBL.

(Ouassia wood, Gele kabbes)

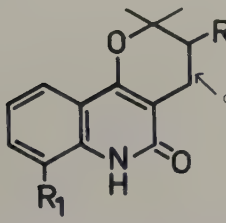
(Leguminosae-Papilionaceae)



Chrysophanol-9-anthrone (R = H)

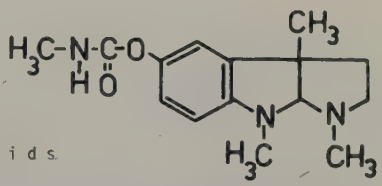
Physcion-9-anthrone (R = OCH_3)

Physcion-10 -anthrone



Flindersine: double bond here

Alkaloids



Flindersine(R_1 = H, R_2 = H) Flindersia australis R.BR.

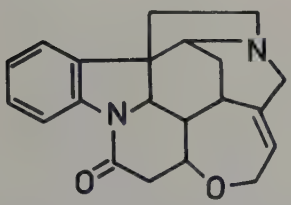
4-Isobalfourodine (R_1=OCH_3, R_2=OH) Balfourodendron riedelianum ENGL.

(Rutaceae)

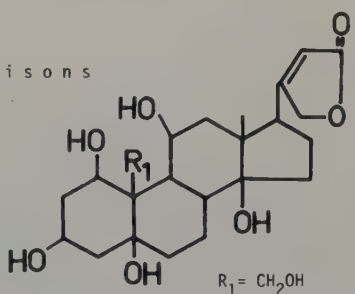
Physostigmine

Hippomane mancinella L.

(Euphorbiaceae)



Arrow poisons



Strychnine

Strychnos spc.

(Loganiaceae)

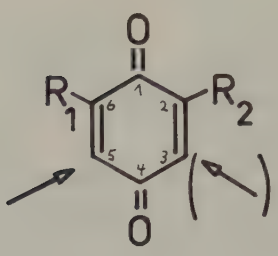
R_1= CH_2OH

g-Strophanthidin = Ouabagenin

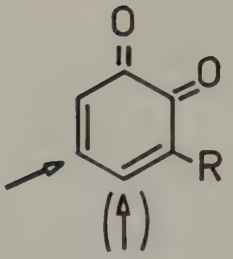
Acokanthera venenata G.DON.

(1,1% in heartwood) (Apocynaceae)

Table 4 Chemical structures of toxic, irritant and sensitising wood constituents not repeated in the following chapters



p-benzoquinone



o-benzoquinone

In *ortho*-quinones like 3-pentadecyl-o-quinone the carbonyl groups and the side chain direct nucleophiles to C-5.

Structure-sensitising relationship studies have also revealed that the length of the side chain in benzo- and naphthoquinones generally has a marked influence on the sensitising power of the compound.
Studies with Poison ivy catechols have led to the hypothesis that an optimum sensitising effect is expected in quinones with a side chain length of about 11 carbon atoms. Shortening or lengthening reduces the sensitising capacity. As all naturally occurring quinones isolated up to now either possess a shorter side chain, e.g. primin (C_5H_{11}) or longer chains, e.g. rapanone ($C_{13}H_{27}$) or are otherwise diminished in their reactivity, e.g. embelin ($C_{11}H_{23}$) by its hydroxy-group in C-6, the synthetic pentadecyl-benzoquinones are the only ones that approach to the ideal structure of an optimum effective contact allergen. Indeed, the catechols respectively their oxidised products are the strongest sensitisers known.

It may be imagined, that the structure of a quinone approaches the ideal form of a sensitiser when it has a reactive 'head' (the quinone ring) and a lipophilic 'tail' (a side chain of 11-13 carbon atoms), because the latter anchors the sensitiser in the lipid layer of the cell membrane while the quinone ring with its reactive sites (C=C double bonds) is presented to the 'antigen binding sites' of the surface antigens (D/DR antigen) of the stimulator cells (Figure 6).

Among the sensitising quinonoid constituents of commercial timbers deoxylapachol (DOL) from Teak is one of the most important ones. Its formula fits well into the hypothesis on structure-sensitising relationships: the C-3 of the quinone ring is available for nucleophilic attack of SH- and NH_2-groups of the HLA-D/DR antigens of epidermal Langerhans cells.

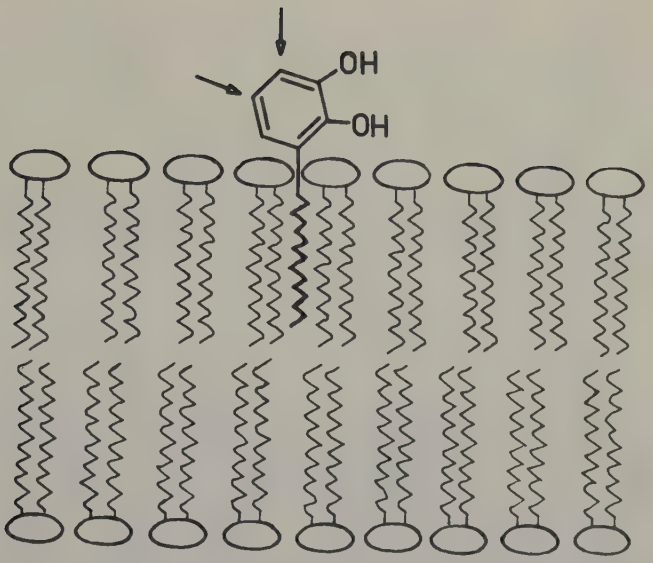


Figure 6 Sensitising compound with its side chain anchored in the lipid layer of the cell membrane of a stimulator cell presenting its reactive sites ('head') to the antigen binding sites of the D/DR surface antigen

During this process the quinone is reduced and subsequently oxidised, e.g. by air, as shown in Figure 7.

Lapachol, differing from DOL only by an additional OH-group, is not able to function as a primary sensitiser (inductor) due to the hydroxyl group at C-3. (If the 'blocking group' was OCH_3, Cl, OAc or *o*-phosphate, etc. it could be replaced by SH- or NH_2-groups). Though Lapachol occurs in markedly higher concentrations in Teak than DOL attempts to sensitise guinea pigs with it have failed. Lapachol can only be considered as a 'secondary allergen' (elicitor) that is able to elicit skin responses in individuals (or guinea pigs) primarily sensitised by Teak, i.e. its constituent deoxylapachol, but it will always fail to induce contact sensitivity.

Evidence for these remarkable differences is shown by the fact that skin reactions with DOL are always 100 - 200 times stronger than with lapachol at equal concentrations. Thus it becomes understandable, that fully substituted benzo- and naphthoquinones may only function as primary sensitisers (inductors) in the case they possess a free position or a slightly separable group at the quinone ring. (Anthraquinones may possibly be changed by patterns of metabolic deviation, e.g. after ingestion, to a benzo- or naphthoquinone structure).

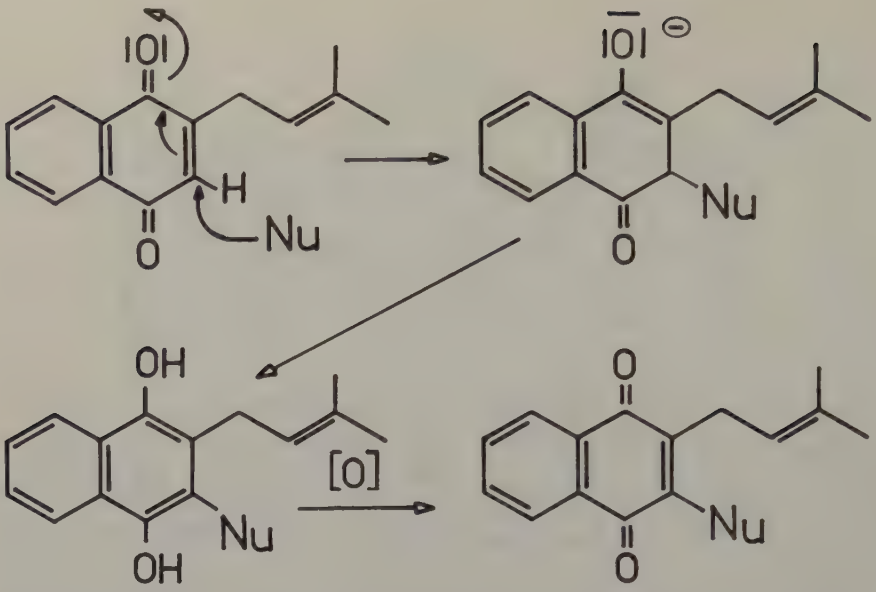


Figure 7 Nucleophilic attack on deoxylapachol during induction of contact sensitivity; Nu = Nucleophile

Cross-reactivities between chemically related quinones derived from plants and woods have been observed in sensitised individuals (see Brazilian rosewood, Pao ferro) and also experimentally in guinea pigs (Schulz et al. 1977, 1979). According to these studies cross-reactivities exist between primin, deoxylapachol, various dalbergiones, mansonones and other quinones. 2-dimethylallyl-benzoquinone derived from the Mediterranean weed *Phagnalon saxatile* (L.) Cass. possesses similar sensitising capacities and cross-reacts with other quinonoid compounds as well (Hausen 1977) (see Figure 5, p. 20).

Quinones of the benzo- and naphthoquinone-type, which are suspected to induce sensitisation, can be detected in wood extracts after thin-layer chromatographic separation by spraying the plates with Craven-solution, giving well defined colour reactions with quinones.

The **Craven-test** is performed by mixing equal amounts (v/v) of absolute ethanol and ammonia (25 %) to which 3 - 5 drops of ethyl cyano-acetate are added shortly before use. The solution is sprayed or poured on the plates giving blue to green colour reactions after a few seconds in the presence of more than 5 μg of the quinone.

In conclusion, benzo- and naphthoquinones, detected in commercial timbers, with at least one unsubstituted carbon atom in the quinone ring (positive Craven-test) and an alkyl side chain must undoubtedly be considered as potentially strong contact allergens.

For all those who are specially interested in naturally occurring quinones the excellent book of Thomson (1971) is recommended.

References

Craven, R.: J.chem.Soc. (1931), 1605
Hausen, B.M.: Planta med. **32**, 287 (1977)
Schulz, K.H. et al;: Arch.Derm.Res. **258**, 41 (1977)
Schulz, K.H. et al.: Arch.Derm.Res. **264**, 275 (1979)
Thomson, R.H.: Naturally occurring quinones. Academic Press: London, N.Y. 1971

Animal experiments

Detailed information on the relationship between chemical structure and sensitising capacity can only be obtained in animal experiments. Determination of the sensitising potency of eczemateous wood constituents is preferably carried out on guinea pigs. This experimental animal model is suitable either for the examination of isolated pure compounds or for crude wood extracts.
For this purpose three sensitisation methods are available: the open epicutaneous method (OET), the maximisation test (GPMT - guinea pig maximisation test) (Magnusson & Kligman 1970) and the optimisation test (Maurer et al. 1975). Usually the OET and the maximisation test are used in our laboratory.
Male or female, but not mixed albino guinea pigs of the Pirbright white strain (or an adequate strain which may be easily sensitised with low molecular weight substances) are used, fed with pellets of a special animal food and water *ad libitum*.

Wood shavings or wood dusts are extracted at room temperature (or by careful heating to 40 - 60 °C) with ethanol, chloroform, ether or ethyl acetate for at least 24 h. In cases where the wood constituents are sufficiently stable a hot extraction (in a Soxhlet apparatus) yields higher amounts of the sensitising constituents. The filtered extract is evaporated to dryness (at reduced temperature) and the residue dissolved in acetone, ethanol or a mixture of ethanol (45 %), methyl glycol M 859 (45 %) and Tween 80 (10 %). Similar vehicles are used for pure compounds.
Concentrations employed for the open epicutaneous method are subtoxic or slightly toxic, i.e. weak primary irritant reactions on the skin of untreated animals produced by a single application.

In all other cases a 10 % concentration of the wood extract or compound is sufficient. Previous to the sensitisation procedure thresholds of primary irritation of the wood extracts or pure compounds are determined by a single application of at least three different concentrations, e.g. 1 %, 3 % and 10 %, to the skin of untreated guinea pigs. Readings are carried out after 24 and 48 hours.

Open epicutaneous method (OET)
0,03 ml of the solution is applied daily (weekends exempted) to a 2 cm^2 test area of the clipped and shaved flank of the animals and equally distributed by means of a glass rod. Applications are continued for a period of up to three weeks but may be interrupted sooner if there is a strong inflammatory reaction (+++) (see p. 15).
Two weeks after the end of the sensitising procedure challenge is carried out by epicutaneous application of 0,03 ml of 3 - 4 different subtoxic (non-primary irritant) concentrations of the wood extract or isolated fraction or pure compound to an area of 2 cm^2 of the *opposite* flank of the sensitised animals. The reactions are read after 24, 48 and 72 hours at constant lightning (Figure 8).

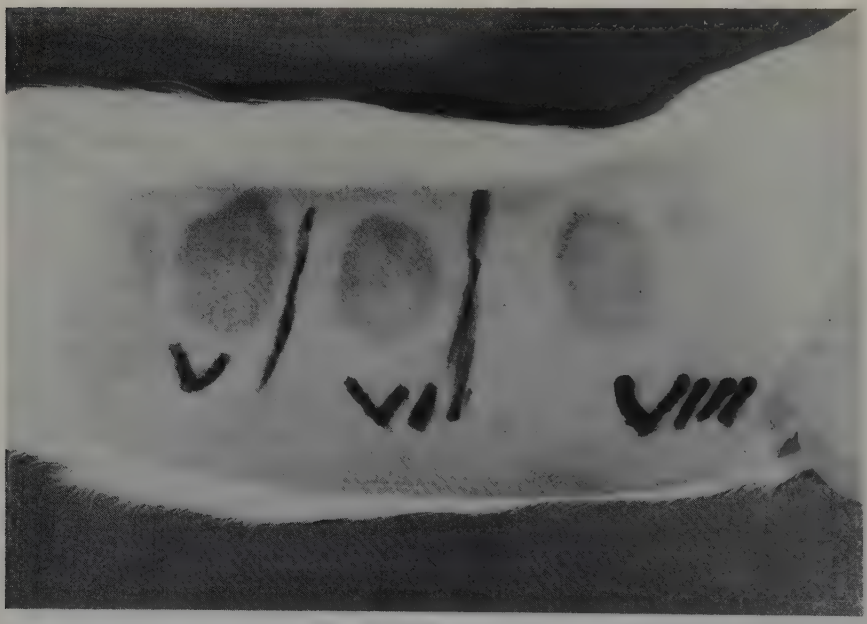


Figure 8 Allergic reactions obtained after challenge with purified isolated constituents on the skin of a guinea pig previously sensitised with a crude wood extract from which the constituents were obtained by chromatographic separation

The intensity of the obtained reactions is evaluated according to the degree of redness (erythema), swelling and exudation of the skin as described on page 15.
In our laboratory the OET has been used most as it corresponds closely to the natural sensitisation conditions of the human skin under the influence of environmental and occupational hazards.

Maximisation test (GPMT)
A row of three injections, six in all, are made in the shoulder region of a clipped and shaved area of 4 x 6 cm where the following are applied:

1. 0,05 ml of Freund's adjuvant without the allergen
2. 0,05 ml of the allergen in phys. saline or oil without Freund's adjuvant
3. 0,05 ml of the allergen emulsified in Freund's adjuvant.

Injections are set intradermal deep into the dermis to minimise sloughing. Allergen concentrations vary from 1 % to 25 %, usually between 5 and 10 %.
Water-soluble allergens are dissolved in water, oil-soluble and pure substances are incorporated into oil (e.g. paraffin) prior to emulsification.
One week later topical application is carried out. 24 hours before a mild inflammatory reaction is produced by treatment with 10 % sodium lauryl sulfate in petrolatum (vaseline) massaged into the skin by a glass rod. The allergen is spread over a 2 x 4 cm patch of Whatman No. 3 MM filter paper incorporated into petrolatum or in 70 % ethanol to saturation. The patch is covered by an overlapping strip of plastic tape and firmly secured for 48 hours by elastic adhesive plastic wound around the torso of the animal.

Challenge is carried out two weeks after the last exposure using three different subtoxic concentrations by open epicutaneous or closed patch test, and read after 24, 48 and 72 hours (Magnusson & Kligman 1970).

Mean response
The mean response is the score calculated by summing the numerical readings (see the right row p. 15) of all challenge concentrations and dividing this by the total number of treated animals.

References

Magnusson, B., Kligman, A.M.: Allergic contact dermatitis in the guinea pig. C.C.Thomas: Springfield, Illinois, 1970
Maurer, T. et al.: Agents and Actions 5, (1975)

Previous reviews

Reviews on irritant and sensitising woods and plants have been published for more than 100 years. One of the first and most excellent reviews is White's 'Dermatitis venenata' of 1887; he was a professor of Dermatology in Boston. A recent well-documented monograph is that of Woods & Calnan (1976).
Generally, the reviews and monographs written before 1930 are unreliable concerning botanical names and chemical structures. Although they are particularly uncritical and contain information on both wood and plant species they have been listed in the following table (Table 5).
Certain reviews consist of little more than a list of toxic woods, but they are included for the benefit of those who are interested in older references.

Table 5 Reviews on toxic, irritant and sensitising wood and plant species

1887	White, J.C.	Dermatitis venenata. Cupples & Hurd: Boston
1887	Cornevin, C.	Des plantes vénéneuse. Firmin-Didot & Cie: Paris
1901	Koelsch,F.	Zschr.Gewerbehyg. Unfallverhüt. **23**, 622
1901	Bretin, P.M.	Contribution à l'étude de l'origine végétale de certaine dermatites. Thesis: Lyon
1910	Grossmann, J.	Bayer.Ind.Gewerbebl. **96**, 51 Der Holzkäufer **100-103**, 529 - 545 (1920)
1912	Brezina, E.	Internationale Übersicht über Gewerbekrankheiten in: Teleky, L. (ed.): Wiener Arbeiten aus dem Gebiet der sozialen Medizin. A.Hölder: Vienna
1914	Cleland, J.B.	Plants, including fungi, poisonous or otherwise injurious to man in Australia. Austr.Med.Gaz. **35**, 541 and 569 Med.J.Austr. **12**, 443 (1925) Med.J.Austr. (1931), 775
1914	Schreiber, E.	Über hautreizende Hölzer. Thesis: Berlin publ.: Ber.dtsch.pharm.Ges. **24**, 385
1922	Ridley, H.N.	J.trop.Med.Hyg. **25**, 225
1926	Broers, H.	in: Die Schädigung der Haut durch Beruf und gewerbliche Arbeit. Ed. K. Ullmann et al. Verlag L. Voss: Leipzig, Vol. **2**, 509
1926	Touton, K.	Zbl.Haut Geschlkrkh. **17**, 713 Zbl.Haut Geschlkrkh. **20**, 833
1928	Lewin, L.	Gifte und Vergiftungen. 4. Book: 5. unchanged edition, K.F.Haug: Ulm, 1962
1932	Freise, F.W.	Arch.Gewerbehyg. & -pathol. **3**, 1 Samml. Vergiftungsfälle C 7, 1 (1936)

		Samml. Vergiftungsfälle C 7, 61 (1936)
		Samml. Vergiftungsfälle C 8, 13 (1937)
1933	Senear, F.E.	JAMA **101**, 1527
1934	Rasch, H.	Int.Labor.Off. **2**, 680 and Hyg.Trav. **22**, 1 (1925)
1935	Bardel, S.	Les dermatoses par bois toxiques. Thesis: Paris
1937	Weber, L.F.	Arch.Derm. **35**, 129
		Arch.Derm. **67**, 388 (1953)
1943	Allen, P.H.	Am.J.trop.Med. **23**, 1
1944	Arnold, H.L.	Poisonous plants of Hawaii. Tongg Publ.Comp.: Honolulu
1948	Webb, L.J.	Guide to the medicinal and poisonous plants of Queensland. Coun.Sci.Ind.Res.Bull. **232**, 1 (Melb.)
1951	Muenscher, W.C.	Poisonous plants of the United States. MacMillan Co: New York
	Conor,H.E.	Poisonous plants in New Zealand. Dept Sci.Ind. Res.N.Z.Bull. No. 11: Wellington, N.Z.
1956	Sandermann, W et al.	Holz als Roh - Werkstoff **14** ,37 and 87
1957	Schwartz, L. et al.	Occupational diseases of the skin. 3rd ed. Lea & Febiger: Philadelphia
1958	Gottwald, H.	Handelshölzer. F.Holzmann: Hamburg
1959	Koelsch, F.	Handbuch der Berufskrankheiten. 2nd ed. Fischer: Jena
1961	Mors, W.B. et al.	Die industriell verwertbaren Pflanzen Brasiliens. Bras. Handelskammer: Sao Paulo
1962	Woods, B.	Trans.St.John's Hosp.Derm.Soc. **48**, 75
1966	Behl, P.N. et al.	Skin-irritant and sensitizing plants found in India. P.N.Behl: New Delhi, private printing
1968	Lampe, K.F. et al.	Plant toxicity and dermatitis. Williams & Wilkins: Baltimore
1969	Rook, A. et al.	Textbook of Dermatology. Blackwell Sci.Publ.: Oxford
1970	Foussereau, J. et al.	Les eczémas allergiques professionnels. Masson & Cie: Paris
1971	Morton, J.F.	Plants poisonous to people. Fairchild Tropical Garden: Florida; 2nd ed. 1977
1972	Roman-Paris, B.	Contribution à l'étude de la pathologie due aux bois. Thesis: Marseille
	Schuerkaemper, H.	Allergie durch tropische Hölzer. Thesis: Munich
1973	Hausen, B.M.	Holzarten mit gesundheitsschädigenden Inhaltsstoffen. 1st ed. DRW-Verlag: Stuttgart (References published privately 1973)
1976	Castagne, D.	Dermatoses professionnelles provoquées par les bois tropicaux. Thesis: Bordeaux

1976	Woods, B. et al.	Toxic woods. Brit.J.Derm. **95**, Suppl. **13**, 1
1978	Belli, S. et al.	Ann.Ist.Super.Sanita **14**, 819
1979	Mitchell, J.C. et al.	Botanical Dermatology. Greengrass: Vancouver

II. Systematic review of irritant, toxic and sensitising wood species of commercial value

For the following review of toxic, irritant and sensitising wood species some general references have been used that are not further mentioned in detail in the following description of each single timber.

External compounds and solvents such as dyes, glues, varnishes, wood preservatives and other material applied to wood after cutting, and thus being not of natural origin are not taken into account.

Anonymous	Informationsdienst Holz. Edited by Verein Deutscher Holzeinfuhrhäuser: Hamburg, since 1972 (Flow sheet-collection)
Anonymous	Förderung afrikanischer Tropenhölzer. Published by the Common Market: Brussels 1977
Bolza, E. et al.	African timbers. CSIRO: Melbourne 1972
Dahms, K.-G.	Afrikanische Exporthölzer. DRW-Verlag: Stuttgart 1968
Farmer, R.H.	A handbook of hardwoods. 2nd ed. HMSO: London 1972
Gottwald, H.	Handelshölzer. F.Holzmann: Hamburg 1958 1st edition
Krauth, E.H.	Holznamenverzeichnis. Th. Nagel: Hamburg 1974
Meniado, J.A. et al.	Timbers of the Philippines. Gov. Printing Office: Manila 1974
Palutan, E.	Monografie di legni con campioni di vero legno. Palutan Editrice: Milano 1975
Pearson, F.G.O. et al.	Timbers used in the musical instrument industry. Forest Products Research Laboratory: Princes Risborough England 1967
Titmuss, F.H.	Commercial timbers of the world. 3rd ed. Technical Press: London 1965

Mitragyna ciliata Aubr. & Pell.
Mitragyna stipulosa O. Kuntze
(Naucleaceae)

Abura
Bahia
Subaha

West African timber, mainly from Nigera, Ghana and Zaire for general purposes, medium weight and small dimensions, used instead of Alder. Uniformly light yellow-brown, plain appearance. Used for drawer sides, frames, shop-fittings, extensively for fitting and decorative mouldings, other interior works and for joinery. In the Netherlands used frequently for manufacturing of clogs.
The fine sawdust has irritant properties. Occasionally complaints of dermatitis, nasal and mucosal irritation have been reported in Nigerian workers (Titmuss 1965, Woods 1976), also vomiting has been observed (Hering 1966, Wagenführ 1961).
The causal factors are unknown, possibly the oxindole alkaloids isolated by Shellard et al. (1974) are involved in the irritant and poisoning properties of Abura.

References

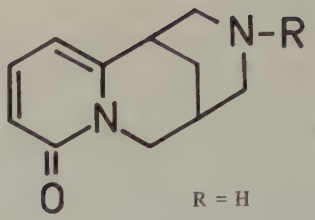
Hering, H.: Derm.Wschr. **152**, 807 (1966)
Shellard, E.J. et al.: Planta med. **25**, 80 and 172 (1974)
Titmuss, F. H. Commercial timbers of the world. Tech.Press: London 1965
Wagenführ, R.: Möbel und Wohnraum **4**, 120 (1961)
Woods, B. et al.: Brit.J.Derm. **94**, Suppl. **13**, 1 (1976)

Pericopsis elata van Meuven
(Legumin. -Papilion.)

Afrormosia
Kokrodua
Asamela

Native to West Africa between Ivory Coast and Zaire. Timber of good appearance and strength properties. Used for exterior and interior work, boat-building, joinery, furniture, flooring, framing, marine constructions, and as decorative veneer in furniture.

Afrormosia is said to belong to the woods which irritate the skin (Hublet 1972, Oleffe 1973, Orsler 1969). Positive patch tests in patients have been recognised by Schleicher (1974), and Woods & Calnan (1976).
Marweg (1968) isolated three alkaloids from the wood, two of them being cytisine and N-methylcytisine. Both have been incriminated for causing cramps and other paralytic symptoms observed in a patient (Hausen 1973). Furthermore afrormosin (= 7-hydroxy-6,4'-dimethoxyisoflavone) has been found in the tree (McMurry 1960). Sensitisation experiments in guinea pigs using the OET were successful.
The responsible agents are not known, though 2,6-dimethoxybenzoquinone could be isolated from the wood, which may function as a sensitiser (see Australian blackwood).



R = H Cytisine
R = CH_3 N-methylcytisine

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Hausen, B.M.: Holzarten mit gesundheitsschädigenden Inhaltsstoffen. DRW-Verlag: Stuttgart 1973
Hublet, P. et al.: Arch.Belg.Med.Soc.Hyg. **38**, 314 (1972)
Marweg, C.: unpublished results, Hamburg 1968
McMurry, T.B.H. et ak.: J.chem.Soc. (1960), 1491
Oleffe, J. et al.: Rev.franc.Allergol. **13**, 65 (1973)
Orsler, R.J.: Timberlab. Papers No. 11, 1 (1969)
Schleicher, H.: Derm.Mschr. **160**, 433 (1974)
Woods, B. et al.: Brit.J.Derm. **94**, Suppl. **13**, 1 (1976)

Afzelia africana SM — *Afzelia*
A. bipindensis Harms — Doussié
A. bella Harms — Linguè
A. bachyloba Harms — Apa
A. quanzensis Welw.
(Legumin. - Caesalpin.)

Native to West and Central Africa. No distinction is made between the different species of Afzelia commercially.
Afzelia is a heavy timber with outstanding stability and durability, used for staircases, door and indoor frames, underframes of road and railway wagons, wooden floors as well as for decorative floors for pedestrian traffic. Not recommended for kitchen and laundry use because it may stain fabrics under moist conditions due to its yellow dyestuff.

Dermatitis has been reported several times (Dantin-Galego 1952, Koelsch 1959, Raymond 1959). In West Africa skin reactions, nasal irritation and sneesing caused by the fine dust have been observed. The responsible agents are unknown.
Bleumink (1974) saw three positive patch tests with Afzelia in woodworkers.

Sensitisation of guinea pigs using the OET was successful (Hausen 1978).

References

Bleumink, E. et al.: Contact Derm.Newslett. No. 16, 436 (1974)
Dantin-Galego, J. et al.: Ind.Med.Surg. **21**, 41 (1952)
Hausen, B.M.: Contact Derm. **4**, 204 (1978)
Hublet, P. et al.: Arch.Belg.Med.Soc.Hyg. **38**, 314 (1972)
Koelsch, F.: Handbuch der Berufskrankheiten. 2nd ed. Fischer: Jena 1959
Oleffe, J. et al.: Rev.franc.Allergol. **13**, 65 (1973)
Raymond, V.: Rev.Pract. (Paris) **9**, 2638 (1959)

Gossweilerodendron balsamifera Harms
(Legumin.- Caesalpin.)

Agba
Tola
Tola branca

Mainly exported from Nigeria, Cameroon, People's Republic of Congo, Angola and Zaire to Europe.
Timber for general purposes, light. Joinery wood for interior and exterior uses, frequently used as an alternative for Oak.
Skin irritations have been described. The wood is generally said to be injurious to health. Two patients with dermatitis patch tested by Woods (1976) gave positive reactions to Agba.
The causal factors are unknown.

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Anonymous: Intern.Holzmarkt **17/18**, 32 (1957)
Heilig, P.M.: Vakbl.voor meubelindustr. **38**, 1440 (1957)
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Jones, J.: Furniture Dev.Coun.Tech.Inform.Serv.Inform.Rep. No. 6 (1946)
Morgan, J.W.W. et al.: IUFRO Proc.Meet.Sec. **41**, Vol. **3**, 1 (1965)
Orsler, R.J.: Timberlab. Papers No. 11, 1 (1969)
Woods, B. et al.: Brit.J.Derm. **94**, Suppl. **13**, 1 (1976)

Alnus glutinosa Gaertn.
(Betulaceae)

Alder
Common or black alder
Erle

Grows in Europe and Western Asia. It is light and soft and therefore easy to work with. Used for toys, general turnery, broom and brush backs.
In 1927 dermatitis of the face and hands was observed in four workers using Alder.

Patch tests with different extracts and Alder tannin were positive and negative in controls (Brügel et al. 1927). The authors suggested one of the tannins might be the sensitisers. Dässler & Urzynicok (1958) confirmed this with the isolated tannin, but got negative patch test results in two *Alder*-sensitive patients.
Two further cases of allergic contact dermatitis of the face, hands and arms were seen in 1974 by Fregert. Epicutaneous tests with the sawdust and the juice pressed from the shavings of the tree were positive, twelve controls negative. No further investigations were carried out, though other authors have reported Alder dermatitis (McCord 1958, Zafiropoulo 1968).

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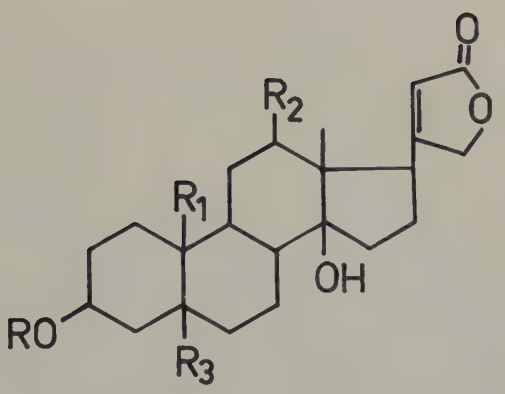
Antiaris toxicaria var. *africana* Lesch.
Antiaris africana Engl.
(Moraceae)

Antiaris
Bonkonko, Oro
Kirundu
Andoum, Upas

Antiaris occurs in West, Central and East Africa. The timber is light yellow-brown, resembling Obeche. It is slightly affected by insects and fungal attacks and therefore must be protected. It is generally used for furniture; polishes with a remarkable golden lustre. Also suitable for carcassing and shelves, frames and mouldings. Veneers sometimes show an attractive stripe.
The sawdust irritates the nose, throat and skin (Baumer 1955, White 1887, Woods 1976). The name 'toxicaria' points to the poisonous properties of this wood. The species of Africa and Asia contain some glycosides with cardiac effects in their latices. The highest amounts are found in the bark.
Five out of the 27 known glycosides of the African species have poisonous properties. Their structures were identified by Wehrli and co-workers in 1962, as shown below.

The toxic properties were examined in animal experiments using cats and dogs. The lethal doses for cats are given on page 39. In its native countries the latices of Antiaris species are used as arrow poison, but it is said that the sap is harmless in man on unbroken skin (Wehrli et al. 1962).



Name	R = Sugar	R_1	R_2	R_3	Lethal dose cat, mg/kg
α-Antiarin	Gu	CHO	OH	OH	0,1164
ß-Antiarin	Rh	CHO	OH	OH	0,1000
Evomonosid	Rh	CH_3	H	H	0,2784
Malayosid	Rh	CHO	H	H	0,1070
Convallatoxin	Rh	CHO	H	OH	0,0789

Gu = 'Gulomethylose', Rh = Rhamnose

References

Baumer, M; Rev.Bois Fôr.Trop. **43**, 27 (1955)
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White, J.C. Dermatitis venenata. Cupples & Hurd: Boston 1887
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Turraeanthus africanus Pellegr. ***Avodiré***
(Meliaceae)

Imported from West Africa, mainly from Ghana and especially the Ivory Coast. Extensively used in decorative veneer production, high-class interior joinery, but also suitable for all kinds of furniture.
Dermatitis, nosebleeding and irritation of the mucous membranes have been reported by Hublet (1972), Oleffe (1973), Peche (1939) and Wagenführ (1967). Positive patch tests were obtained with the sawdust in three cases by Woods (1976).

Calnan (1970) observed a positive patch test (++) in a 43 year old cabinet maker with a nine months old dermatitis of the hands, arms and sides of the neck, but the patient also reacted to some other wood dusts and plant material.
The responsible agents are unknown.

References

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Hublet, P. et al.: Arch.Belg.Med.Soc.Hyg. **38**, 314 (1972)
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Distemonanthus benthamianus Baillon — ***Ayan***
(Legumin.-Caesalpin.) — Movingui

Imported from West Africa, mainly Cameroon and Nigeria. A decorative yellow smooth and heavy timber with good dimensional stability. Suitable for the same purposes as Oak, e.g. door frames, windows, cabinet working. In England mainly used for cab bodies. Suitable also for domestic flooring, but not recommended for kitchen and laundry equipment because of its yellow dye-stuff, which may stain fabrics.
Termite resistant. Import is still restricted, but it is said that this wood has a future.

Morgan & Thomson (1967) reported a case of severe dermatitis recurring for four years in a carpenter engaged in making coffins. Patch tests were positive with the sawdust and two of the four isolated flavonoids (King 1952, 1954). Allergic reactions were observed with oxyayanin A (++++) and oxyayanin B (+++).
Thirteen further cases of Ayan dermatitis have been recently described by Woods & Calnan. One case was observed by Orsler in 1969.
It cannot be excluded that other still unknown contact allergens occur in the wood besides the flavonoids mentioned.
For structures see next page (p. 41).
The two other flavonoids ayanin and distemonanthin must be considered as minor allergens.

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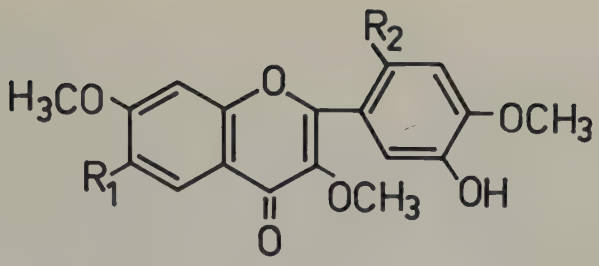
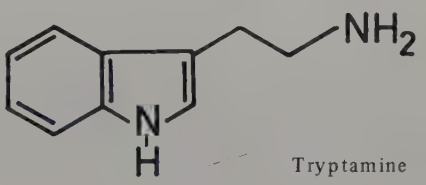


Oxyayanin A (R_1 = H, R_2 = OH)
Oxyayanin B (R_1 = OH, R_2 = H)
Sensitising flavonoid constituents of Ayan (*Distemonanthus benthamianus* Baill.)

Dicorynia guianensis Amshoff
(= ***Dicorynia paraensis*** Bentham)
(Legumin.- Caesalpin.)

Basralocus
Angélique
Angelim

Imported from South America, mainly from Surinam, French Guinea and Brazil.
The colour varies from darker to lighter types ('Angélique gris'). A good timber for marine constructions, docks, lock gates and other harbour works due to its extreme resistance to marine borer decay. Also suitable for other construction works where good strength properties are needed, e.g. bridge flooring and railway sleepers. Because of its resistance to acid also used for barrel and vat staves.
Though no description of cases are known, the wood is generally suspected to be toxic (Baumer 1955).
The resistance against marine borer attacks is due to the occurrence of two alkaloids, one of which has been identified as tryptamine (0,05 %) (Sandermann et al. 1967). It may be suggested that these alkaloids are responsible for the injurious properties of the wood dust, as tryptamine is known for its poisonous effects.



Tryptamine

References

Baumer, M.: Rev.Bois Fôr.Trop. **43**, 27 (1955)
Sandermann, W. et al.: Holzforsch. **21**, 154 (1967); Naturwiss. **10**, 249 (1967)

Castanospermum australe A. Cunn.
(Legumin.- Papilion.)

Black bean
Moreton Bay Chestnut
Queensland red bean

This tree from Eastern Australia is not exported, but used moderately in Australia. Recent information indicates that it is also cultivated in South Africa due to its resistance to termite attacks (Francis et al. 1967).
Based on its attractive appearance most of the production is veneer, but there are uses as solid wood for joinery, furniture and interior fittings too.
Irritation of the mucous membranes has reported in 1909 by Maiden and Greshoff. Later reports originate from Aldersey (1925) and Chittenden (1931).
Our own attempts to sensitise guinea pigs using the OET and a 10 % ethanolic extract of the wood failed. A fraction obtained by chromatography gave a positive colour reaction with the Craven-test (see p. 28), which possibly contained a quinone. But this compound was unstable and gave no evidence of sensitising properties (unpublished results).
Black bean also contains two physiologically active saponins, castanogenin (medicagenic acid) and bayogenin, as well as the isoflavones formononetin (7-hydroxy-4'-methoxyisoflavone) and afrormosin (= castanin) (7-hydroxy-6,4'-dimethoxyisoflavone) (Eade 1963, 1966)

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Fagus sylvatica L.
(Fagaceae)

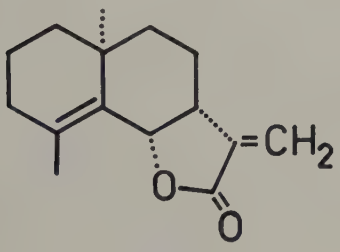
Beech
Buche
Hêtre

Beech is the most extensively used native wood species in Central Europe. The largest consumer is the furniture industry. When Beech is steamed it gives a pinkish colour which is preferred for special purposes, such as bobbins, brush backs and handles, domestic woodware.
Its strength makes is suitable for such furniture as school desks and chairs. Generally it is used for tool handles, knife-handles, sports goods and special parts of musical in-

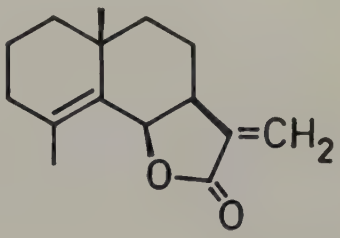
struments. In Denmark and West-Germany often used for flooring. Plywood is frequently made from Beech and exported.

Many cases of Beech dermatitis (so-called 'wood cutter's disease') are caused by liverworts and lichens growing on the bark of Beech trees. Most of them belong to the genera *Parmelia, Frullania, Cetraria, Cladonia, Usnea* and others, and contain besides other compounds sesquiterpene lactones with sensitising properties, such as frullanolide in *Frullania* species (Mitchell 1965, 1969; Suire 1976, Tenchio 1948).

Though it seems now doubtful whether real eczematous dermatitis can be induced by contact with the sawdust of Beech its occurrence must be considered (Fisher 1967, Howes 1951, Malespine 1935, Urbach 1949).



(+)-Frullanolide



(-)-Frullanolide

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Tabebuia serratifolia Nichols.
(Bignoniaceae)

Bethabara
Surinam groenheart
Pau d'Arco
Guaycán

Imported from South America in small amounts, mostly from Columbia, Venezuela

Guyana and other countries of the northern part of South America, including Brazil. The timber has good strength properties and high resistance to decay. Used for sports equipment and handles, similar to the use of Hickory. Frequently used in wood pulping machines as 'knife holders' (Garrat 1922).

Allergic contact dermatitis was described in 1967 by Weitbrecht. A joiner developed dermatitis of the face and hands lasting for two weeks after cutting, planing and sanding of Bethabara 'knife holders'. Four years later the dermatitis recurred when he worked again with this wood.

Our chemical investigations of the wood and following epicutaneous tests with isolated constituents in Weitbrecht's patient provoked positive test reactions; the obtained compounds were identified as lapachol and deoxylapachol (see Teak), the latter being responsible for the observed dermatitis (Hausen et al. 1971).

Lapachol and deoxylapachol are moderately distributed quinonoid constituents, with eliciting (lapachol) and sensitising (deoxylapachol) properties, in different *Tabebuia* and *Tecoma* species, which only rarely reach foreign timber markets.

Among these are found:

Tabebuia avellanedae Lor. ex Griseb. (Burnett 1967, Cordero 1951)
Tabebuia pentaphylla Hemsl. (Zafiropoulo 1968)
Tecoma chrysotricha Mart. (Ipé tabaco) (Freise 1932)

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Hausen, B.M. et al.: Berufsderm. **19**, 324 (1971)
Weitbrecht, U.: Berufsderm. **15**, 183 (1967)
Zafiropoulo, A. et al.: Folia Allergol. **15**, 396 (1968)

Betula papyracea Ait
(= ***B. papyrifera*** Marsh.)
Betula alba L.
Betula verrucosa Ehrh.
(Betulaceae)

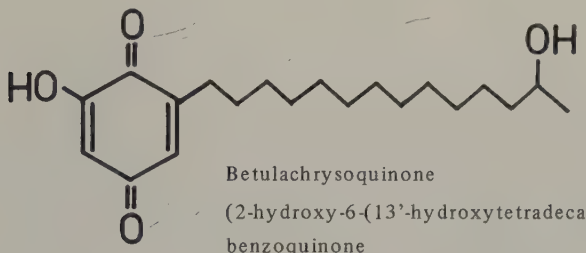
Birch
Paper birch
White birch
Birke

Paper birch grows in the United States and Canada, while White birch originates from Western and Eastern Europe.

The wood is widely used in furniture and decorative veneer production, as well as for pulp and paper.

In 1927 Duke observed two lumbermen with recurring dermatitis of the face and hands after sawing Birch. Positive patch tests were seen by him and also by Woods &

Calnan (1976). Further cases of contact dermatitis are mentioned by Coca (1931), Fisher (1967) , Howes (1951) and Senear (1953).
Cases of skin eruptions are rare, their source is unknown.
Sometimes Birch wood contains a quinone (betulachrysoquinone), which is a *fungal metabolite* (Chen 1977), decayed by *Phanerochaete chrysosporium* Burds.



Betulachrysoquinone

(2-hydroxy-6-(13'-hydroxytetradecanyl)-1,4-benzoquinone

Not a natural wood constituent, but present in the wood after fungal attack

References

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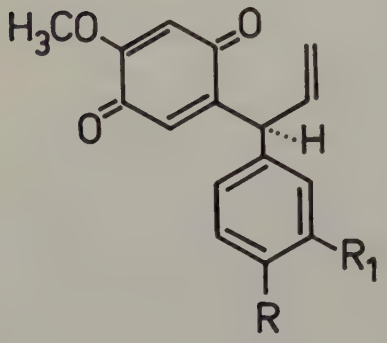
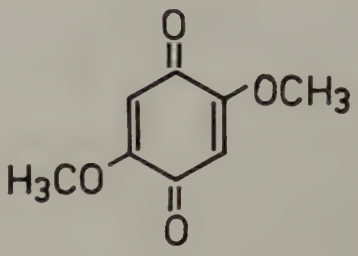
Dalbergia melanoxylon Guill. & Perr.
(Legumin.- Papilion.)

Blackwood, African Grenadill, Pau Preto Mozambique ebony

This hard and heavy, blue-black coloured wood is mainly imported from East Africa (Sudan, Mozambique, Zimbabwe, Togo, Senegal). It causes considerably difficulties in working, especially rapid blunting of saws, but it is excellent for turnery, finishes well and is resistant to termites. It is used primarely for woodwind instruments such as flutes, clarinets, oboes, chanters of bagpipes, and some types of recorders, and also for knife-handles, brush backs, chessmen, truncheons, and other turnery and ornamental purposes.
Cases of dermatitis and conjunctivitis have been observed by Meister (1934), Moll (1950), Nestler (1924), Weber (1937), and recently two cases in clarinet-makers by

Woods & Calnan (1976) who also obtained positive patch tests with the sawdust. Chemical investigation of the wood yielded two quinones of the dalbergione type, namely S-4-methoxydalbergione, S-4'-hydroxy-4-methoxydalbergione and S-3'-hydroxy-4,4'-dimethoxydalbergione (Donnelly 1969, 1975; Hausen 1970), which are known for their sensitising properties, and thus must be considered as the responsible agents (Schulz et al. 1979). 2,5-Dimethoxy-1,4-benzoquinone was also detected, but revealed no sensitising potency (see Macassar).





2,5-Dimethoxy-1,4-benzoquinone

S-4-methoxydalbergione $R = R_1 = H$
S-4'-hydroxy-4-methoxydalbergione $R = OH, R_1 = H$
S-3'-hydroxy-4,4'-dimethoxydalbergione $R = OCH_3, R_1 = OH$

References

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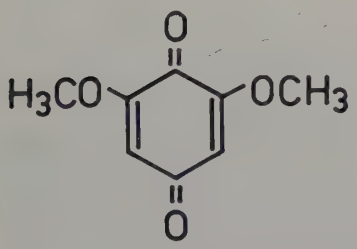
Acacia melanoxylon R.Br. ***Blackwood***, Australian
(Legumin.- Mimos.)

Blackwood is a West Australian timber of dark brown colour, fine and decorative, used for high-quality furniture, panelling, shop and bank fittings, interior joinery, bench work in coach and boat-building, handles and ornamental turnery, musical instruments (sound boards). Mainly used in its native country Australia, but occasionally exported in small quantities to Europe.

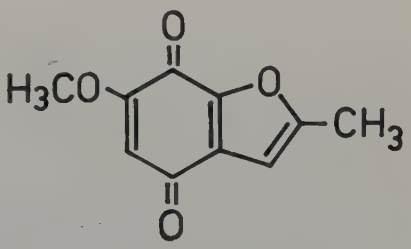
Nott (1925) suffered from a rash of his hands and forearms after handling this wood himself. Nose-bleeding and bronchial asthma were recognised by Pulleine in 1925. Cleland (1925, 1931) observed several cases of weeping dermatitis in joiners and boat-builders (face, neck, forearms) connected with severe itching and conjunctivitis. Robertson (1927) saw one case of asthma and nine cases of contact dermatitis. Though his patch tests remained negative he suggested that sensitisation must play a role.

Further observations with positive patch test results have been contributed by Behl in 1966 and Burry in 1969 and 1973.

An intensified study of Australian blackwood samples by animal experiments and chemical separation of its constituents revealed a moderate sensitising potency. Contact allergy is due to two (three ?) quinonoid wood components. The main contact sensitisers were isolated, and identified by X-ray analysis. The first quinone obtained was 2,6-dimethoxy-1,4-benzoquinone (Schmalle et al. 1977, Hausen 1978). The second quinone was identified as 6-methoxy-2-methyl-benzofuran-4,7-quinone and has been named acamelin (Schmalle & Hausen 1980). This substance belongs to the rare group of furanoquinones which show some similarities to the furanonaphthoquinones of White peroba (*Paratecoma peroba* Kuhlm.) (see p. 101).



2,6-Dimethoxy-1,4-benzoquinone



Acamelin

While 2,6-dimethoxy-1,4-benzoquinone exhibits a relatively weak sensitising capacity when compared with other naturally occurring quinones (see Macassar), acamelin

showed a stronger sensitising effect in the guinea pig experiments (Hausen & Schmalle 1981).
A third quinone only was found occasionally in the five samples of *Acacia melanoxylon* investigated from different places in Australia and thus its relevance as a contact sensitiser may be neglected.

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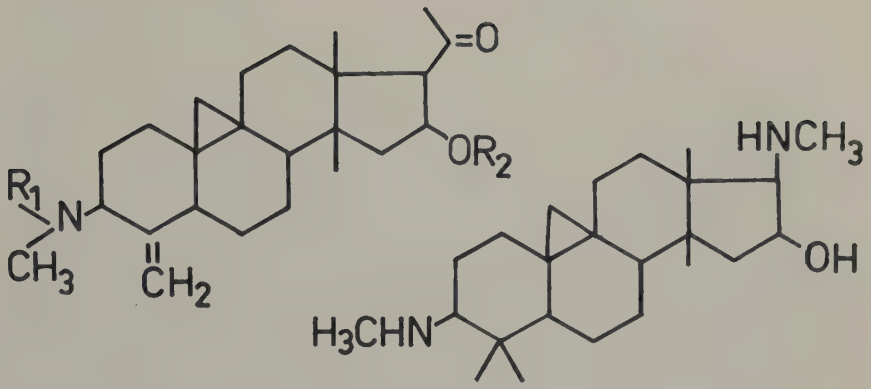
Buxus sempervirens L.
(Buxaceae)

Boxwood, European Buchsbaum

Grows in Europe, Western Asia and North Africa. According to origin named Iranian, Persian, Turkish boxwood etc. Used for tool handles and shuttles in the silk industry. Famous for musical instruments, especially recorders and flutes, when old and dry. Occasionally used for chinrests of violins and other small fancy turnery.
Dermatitis, skin irritations and asthma have been described by some authors. Markin (1930) obtained a positive scratch test in a watchmaker who suffered from asthma when cleaning gold articles with Boxwood sawdust. A similar case was recognised by Walker (1919). Nordin (1947) observed eczema during manufacturing of rulers from Boxwood. Grossmann (1920) mentioned two cases with mild general symptoms.
None of these cases is convincing. Test in control persons are not mentioned. It must be suggested that irritant dermatitis occurred.
The Boxwood alkaloids, which only occur in traces in the wood itself (Dolejs 1965, Tomko 1964, Voticky 1965), may possibly have played a role as poisons or primary irritants. By no means can they be regarded as contact allergens; rather they may function as histamine liberators.
As no further cases have been described in the last 40 years dubious botanical identification concerning these Boxwood cases may be suspected.



Buxtanin $R_1 = R_2 = H$

Buxpiin $R_1 = CH_3, R_2 = H$

Bebuxin
=Cyclovirobuxin D

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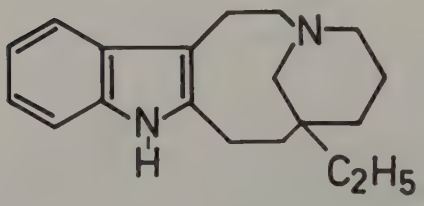
Gonioma kamassi E.Mey
(Apocynaceae)

Boxwood, Knysna
Kamassi

Native to South Africa (Cape Province). Similar to and used as a substitute for European boxwood especially for shuttles, fancy turnery and engraver's work.
Several times it has been reported that the sawdust causes pain and inflammation of the eyelids and nose, dilatation of the pupils of the eyes, and symptoms resembling those of bronchial catarrh, dizziness, dryness of the throat, headache, sleepiness, etc. in men engaged in sawing and sand papering of rulers and shuttles (Hay 1907, Legge 1907).
In 1906 Gibson isolated an alkaloid with curare-like properties from a wood sample, identified as *Sarcocephalus diderichii* Wildemann (= *Nauclea trillesii* Merr.) today

named Bilinga. But this piece of wood was in fact *Gonioma kamassi*. In 1911 Dixon examined the pharmacological action of this alkaloid. He suggested that the symptoms were more related to an 'idiosyncrasy' than a direct poisoning. More than 40 years later the alkaloid kamassin was isolated from the bark of *G. kamassi* and shown to be identical with quebrachamine. We do not know whether this compound was identical with Dixon's alkaloid of 1911 or not. Quebrachamine has curare-like effects upon the nerves (Dixon 1924).

Until 1954 no more than five cases of Boxwood poisoning were observed (Mackenna). This is probably due to the fact that Knysna boxwood is being slowly replaced by substitutes such as Maracaibo boxwood (*Gossypium praecox* P.Wils., Flacourtiaceae), San Domingo boxwood (*Phyllostylon brasiliensis* Cap., Ulmaceae), American cornel (*Cornus florida* L., Cornaceae) and Persimmon (*Diospyros virginiana* L., Ebenaceae). In the 1920 - 1930's occupational dermatitis caused by Knysna boxwood was compensated by law only in Minnesota (USA) (Ganzoni 1929).



Quebrachamine = Kamassin

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Guibourtia tessmannii J.Leonard
Guibourtia demeusei (Harms) J.Leonard
(Legumin.- Caesalpin.)

Bubinga
Kevazingo

Bubinga is imported from West Africa, especially from Cameroon. Only timber shipped from Gaboon is named Kevazingo. In England and West-Germany used chiefly because of its attractive appearance as a veneer for decorative panelling and inlay work. Used also for high-class furniture, fancy turnery, knife-handles and brush backs.
Only verbal information about dermatological risks is available.

Our own sensitising experiments in guinea pigs were successful with an ethanol extract of the wood (GPMT - see p. 29). The crude extract yielded four quinones which all gave positive test responses in the sensitised animals. The quinone with the highest R_F-value elicited the strongest reaction. One of the quinones could be identified as 2,6-dimethoxy-1,4-benzoquinone (see Australian blackwood) (Hausen 1978). On testing this compound gave a weak reaction (one plus). The structures of the remaining quinones are still unknown (unpublished results).

The near related species *Guibourtia arnoldiana* J.Leonard, called Mutenye, is alleged to cause skin lesions as well. Mutenye is imported mainly into Belgium where it is used as a substitute for Walnut.

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Machaerium scleroxylum Tul.
Machaerium spc.
(Legumin.- Papilion.)

Caviuna vermelha
Pao ferro, Moradillo
Jacaranda pardo
Santos Palisander

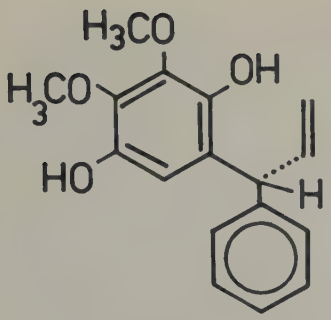
Caviuna vermelha or Pao ferro resembles Brazilian rosewood (*Dalbergia nigra* All.) in its appearance and is closely related to *Dalbergia* species, thus it is frequently used as a substitute and often mistaken for real Rosewood.
However, Caviuna vermelha is considerably more irritant and sensitising than Brazilian rosewood itself.
Outbreaks of dermatitis were observed in 1968 by Morgan et al. and single cases were reported by Hjorth (1974), Holst (1976), Maibach (1970), Orsler (1969) and Phillips (1966). Also in its native country, Brazil, allergic contact dermatitis from Pao ferro is not unknown (Miranda-Bastos 1962).
In Norway recently (1977) six workers became sensitive after a two-week contact with Moradillo. At least 35 cases have been observed in West-Germany in the last two

years (Hausen, in preparation) and five in Madrid (Conde-Salazar et al. 1980). Patch tests were positive in more than 75 % of the woodworkers confronted with the sawdust. The wood samples placed at our disposal yielded up to 2 % of the sensitiser. In most cases the wood species had been sold under the misleading name 'Santos Palisander' or 'Palisander rosé'.
One of the recently observed cases occurred in a 12 year old girl which developed severe perioral dermatitis with swelling of the lips after playing a recorder, manufactured from 'Palisander rosé', for two years. In a first experiment a strong positive reaction (+++ - ++++) was obtained after tying the whole instrument with a plaster to the upper arm of the young girl for 24 hours.
After botanical identification of the recorder wood as *Machaerium scleroxylum* strong positive reactions were obtained with the main sensitiser R-3,4-dimethoxydalbergione (0,1 %) as well as cross-reactions with the related compounds 4-methoxydalbergione (racemate) and S-4 4'-dimethoxydalbergione. After the recorder had been replaced by an Olive wood recorder no further complaints were heard. The Olive wood had been tested epicutaneously before without giving a (cross-) reaction.

The contact sensitisers of Caviuna vermelha are R-3,4-dimethoxydalbergione and its quinol (Eaton et al. 1965, Gottlieb et al. 1964, Morgan et al. 1968).
Sensitisation experiments in guinea pigs (OET) with four different dalbergiones revealed that R-3,4-dimethoxydalbergione possesses the *highest sensitising power* of all dalbergiones (Schulz et al. 1979). Cross-reactions between the related dalbergiones were also disclosed. Cross-reactions to 4-methoxydalbergione (racemate), S-4,4'-dimethoxydalbergione and S-4'-hydroxy-4-methoxydalbergione were seen in most of the patients allergic to Caviuna vermelha mentioned above.

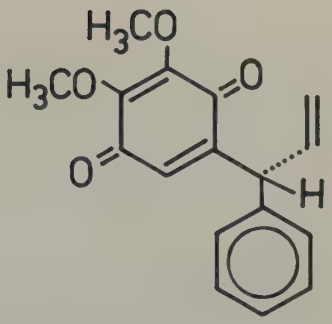
As often experienced with strong sensitisers, R-3,4-dimethoxydalbergione is a primary irritant in concentrations of 1 %. Only dilutions to 0,1 - 0,01 % produce real allergic reactions in sensitised persons and remain negative in controls. It must be emphasised that R-3,4-dimethoxydalbergione only occurs in *Machaerium* species and has not been found in the related *Dalbergia* species.
According to Morgan et al. (1968) Caviuna vermelha contains about three quarters of the sensitiser in form of the quinol and one quarter as the quinone. The quinol is easily oxidised to the corresponding quinone during extraction, separation or by an oxidising chemical.

Some related *Machaerium* species also have been described as the source of allergic contact dermatitis. The following table lists all the species in which R-3,4-dimethoxydalbergione has been discovered as the causative factor.
The sensitising capacity of another *Machaerium* constituent-mucroquinone-is unknown.

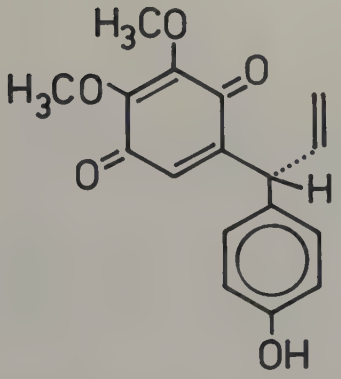


R-3,4-dimethoxydalbergione quinol

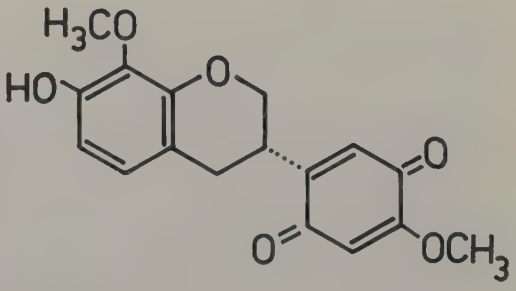
oxid.



R-3,4-dimethoxydalbergione



R-3,4-dimethoxy-4'-hydroxy-dalbergione



Mucroquinone

Species	Dermatitis described	Evidence for R-3,4-dimethoxydal.
Machaerium schomburghkii Bentham	Grossmann 1910	-
(Jacarandá, Ximbo)	Hanslian 1960	-
M. pedicellatum Vog.	Ogiyama 1973	Ogiyama 1973
('Jacarandá')		
M. kuhlmannii Hoehne *	-	Ollis 1978
('Jacarandá')	-	-
M. nictitans (Vell.) Bentham*	-	Ollis 1968
('Jacarandá')	-	Ollis 1978
M. violaceum Vog.	Freise 1932	-
(Orelha d'onca, Knyswood)	Reinl 1965	-

M. villosum Vog.	-	Braga de Oliveira
(Jacaranda paulista)	-	1968
M. mucronulatum Mart. ex Benth.**	-	Kursawa 1968, 1978

* contains also R-4'-hydroxy-3,4-dimethoxydalbergione
** contains mucroquinone

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Cedrela odorata L. — ***Cedar***, Central American
(= ***Cedrela mexicana*** M.J.Roem.) — Cedro
Cedrela fissilis (L.) Vell. — South American cedar
(Meliaceae)

Occurs from Mexico through Central America to the South, except Chile and the West Indies. The related *Cedrela toona* Roxb. grows in South East Asia and Australia. It is also shipped to Europe under the name Burma cedar, Toon or Toona and used for the same purposes as the Central American cedar.

Australian timber varies in colour from pale pink-brown to dark reddish-brown. It resembles some types of Mahogany. All species are characterised by a distinct fragrant scent. The timbers are mainly used in their native countries and little is exported.

Timbers coming to Europe are suitable for cabinet making, interior joinery and panel-

ling; sometimes employed for plywood in England. The heartwood of the South-American cedar is extremely resistant and therefore recommended for planking, boat-building and for the skins of racing boats and canoes. Also used for cigar boxes. Specially employed for sound boards of organs.
Allergic contact dermatitis has been described by Schleicher (1974) caused by *Cedrela toona* who also obtained positive patch tests with the sawdust. Woods & Calnan also have knowledge of some reports of skin irritations.
Several triterpenoid constituents of the heartwood have been isolated and identified by Chan (1972), Hodges (1963), Nagasampasi (1975) and Zelnik (1971), but they cannot be considered as contact allergens.
Our own investigations revealed the occurrence of 2,6-dimethoxy-p-benzoquinone in the heartwood of the Central American species and in Burma cedar (Hausen 1978); it may play a subordinate role as a sensitiser (see p. 47).
Other unknown constituents may be suggested as further sensitising agents in the cedar species.

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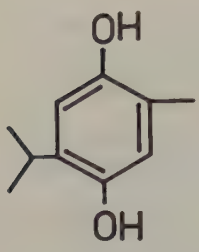
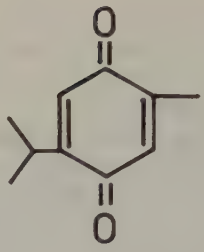
Calocedrus decurrens (Torr.) Florin — ***Cedar***, Incense
(= ***Heyderia decurrens*** (Torr.) K.Koch
(= ***Libocedrus decurrens*** Torr.)
(Cupressaceae)

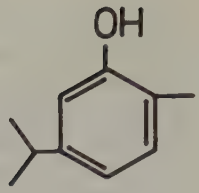
A tree native to California, used frequently for pencil manufacture and locally for fence posts, boarding, venetian blinds, chests and toys.
Two cases of contact dermatitis of the hands have been described by Calnan (1972). In a female clerk the eczema developed between the middle and the ring finger of the right hand, where she used to hold the pencil. Later on the dermatitis spread out to the left arm, the chest, face, tighs and calves. In the second case a contact eczema developed behind the ear, where the pencil was kept.
In both patients strong positive patch tests were obtained with thymoquinone and thymoquinol, weak reactions with carvacrol and a negative one with the three thujaplicins.



Thymoquinol



Thymoquinone



Carvacrol

Incense cedar contains about 32 % carvacrol, 1 % thymoquinol, 4 % thymoquinone and about 3 % of α-, ß- and γ-thujaplicin (Anderson et al. 1965).
Positive patch tests with a 0,1 % concentration of thymoquinone were also obtained by Bleumink (1974) in a patient.
Investigations in our laboratory disclosed thymoquinone as a relatively strong sensitiser (see Western red cedar). Cross-reactions are to be expected due to the chemical relationship of the structure with other known quinonoid sensitisers. The threshold of primary irritation is between 0,3 and 1 %. Thus patch tests only should be carried out with concentrations not exceeding 0,1 %.

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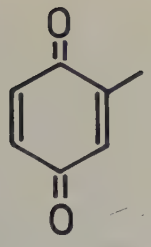
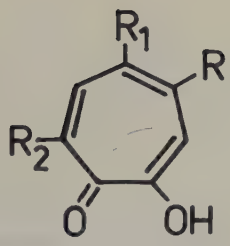
Thuja plicata Donn ex D.Don
(= ***Thuja gigantea*** Nuttal)
(Cupressaceae)

Cedar, Western red
Arbor vitae
Rotzeder

A tree native to the West coast of the United States, but exported all over the world, especially to Australia and Japan. A timber of good stability, useful for interior and exterior constructions, venetian blinds, shingles, buildings, boat-building, planking, panelling and framing.
Besides many cases of bronchial asthma due to the sawdust (see next chapter) some observations of allergic contact dermatitis have been reported by Bleumink (1972, 1973, 1974), Burry (1973), Mitchell (1974) and Orsler (1969). Bleumink got positive patch test results with γ-thujaplicin, thymoquinone, methyl-1,4-benzoquinone and 7-hydroxy-4-isopropyltropolone, thymoquinone giving the strongest response (see above).



Methyl-1,4-benzo-quinone



7-hydroxy-4-isopropyltropolone
$R = H, R_2 = OH, R_1 = -CH(CH_3)_2$

ß-thujaplicin $R = -CH(CH_3)_2$, $R_1 = R_2 = H$

γ-thujaplicin $R = R_2 = H$, $R_1 = -CH(CH_3)_2$

Already in 1967 Suskind succeeded in sensitising guinea pigs with an extract of Western red cedar. Maiden also mentioned a *Thuja* species as early as 1904 in a list of 18 plants causing dermatitis. Grossmann (1910) suspected *Thuja gigantea* to be injurious to health.

Sensitisation of guinea pigs using the maximisation test (GPMT) (see p. 29) with ten different naturally occurring quinones demonstrated that thymoquinone developed the the highest sensitising capacity in the animals. Positive test responses were obtained down to dilutions of 0,01 % (Buske 1974, Hausen 1978) (see also Macassar).

According to Bleumink (1974) the threshold of primary irritation of thymoquinone lies at 0,3 % in man; he therefore recommended testing with 0,1 % dilutions. Calnan (1972) tested his patients with a 1 % concentration and declared the responses to be allergic ones. Probably his thymoquinone sample (commercial thymoquinone is impure) was contaminated, thus he got no primary irritant reactions. Besides that Calnan obtained a positive reaction to ß-thujaplicin.

Our own experiments in guinea pigs of the Pirbright white-strain showed 0,3 % concentrations to be not primary irritant, but patch tests with the same concentration in non-sensitive controls gave a weak response.

However, animal experiments using another guinea pig strain produced no irritant reactions up to 1/10 molar concentrations (= 1,64 %).

These discrepancies may be avoided by patch testing always with a 0,1 % dilution.

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Castanea sativa Mill.
(Fagaceae)

Chestnut, Sweet
Spanish chestnut
European chestnut

Grows in Europe, North Africa and the Near East. Resembles Oak in its appearance. Is used for furniture, ornamental bowls, kitchen utensils, walking sticks, umbrella handles, veneers, fences, gates, railroad sleepers, boat-building. Extraction of tannins is common in some countries.
Dermatitis of the hands in woodmen working with Chestnut in the forests has been described as ' main de crocodile' in the 1930's (Horand 1907, Navarro Martin 1932, Senear 1933, Spillman 1931). It is suggested, however, that all these symptoms of dermatitis were not due to the wood itself, but probably to the occurrence of liverworts and lichens occurring on and in the bark of the trees. These *Frullania* and *Parmelia* species contain sensitising agents which have been identified as sesquiterpene lactones (Mitchell 1965, 1969, Tenchio 1948) (see Beech p. 42).
There is only slight evidence that the wood itself contains any sensitising substance.

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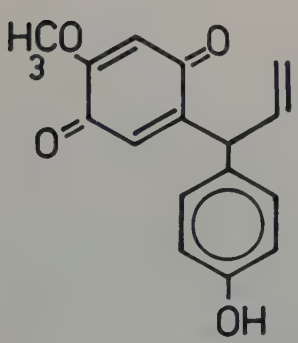
Dalbergia retusa Hemsl.
(= *Dalbergia obtusa* Lec.)
(Legumin.- Papilion.)

Cocobolo

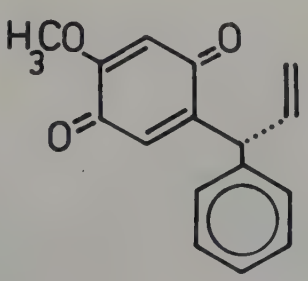
Between the end of the last century and the Second World War Cocobolo was imported from Central America, especially from Nicaragua, Costa Rica and Panama in great quantities. Today very little is exported. The heartwood is characterised by a yellow to reddish-orange, later deepening to a rich-brown or rose colour, marked with numerous irregular concentric markings of black or deep purple. The wood is strong, hard,

compact and fairly heavy, easy to work and of extreme durability. Oily substances make it resistant to the influence of moisture, even when left in contact with water. Great demands for Cocobolo come from manufacturers of knife-handles, brush backs and small tool-handles. Cocobolo holds a supreme position in the cutlery trade. Other uses are the manufacture of chessmen, scientific instruments, butts of billard cues, wooden bracelets and interior turnery.
Today wood suppliers in West-Germany complain about the difficulties in obtaining sufficient Cocobolo from South America due to the reduced exports and rising prices.

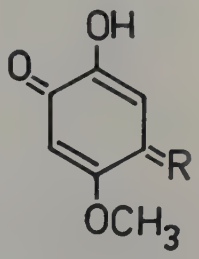
Formerly Cocobolo was used especially in musical instruments, above all for flutes, recorders, clarinets, oboes, etc. At least 25 references can be cited from the literature dealing with allergic perioral dermatitis and swelling of the lips in record players or localised eczema from contact with knife-handles and bracelets. 90 % of all recorders manufactured before World War II in Germany were made from Cocobolo. However, these instruments caused perioral dermatitis in so many cases that the use of the wood had to be abandoned after 1945. Detailed descriptions of dermatitis in workers involved in hairbrush production (Mackee 1913), knife-handle manufacture (Howell 1946, 1950) and recorder turnery and use (Leider 1950, Modlmayer 1931, Steinbrink 1950) have been reported. Though production of recorders from Cocobolo has nearly ceased, one firm in Switzerland still offers decorative and high quality recorders. A questionaire to the manufacturer revealed that only ten complaints of perioral dermatitis had been made by his customers in the last 30 years (priv. comm.).
In 1962 Schulz & Dietrichs patch-tested some allergic turners with three quinones isolated from the wood by Sandermann et al. (1960) which revealed by their positive responses that these quinones were the contact sensitisers of Cocobolo.
Some years later the quinonoid constituents were identified as members of the new class of dalbergiones (Eyton et al. 1965).



S-4'-hydroxy-4-methoxy-dalbergione



R-4-methoxydalbergione



Obtusaquinone
R = CH=CH-Ph
(Ph = Phenyl)

Their sensitising capacity was examined in 1979 by Schulz et al. in animal experiments. Besides the dalbergiones, another constituent - obtusaquinone - also disclosed sensitising power in animal experiments (maximisation test) (Buske 1974) (see also Macassar).

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Brya ebenus DC
(Legumin.- Papilion.)

Cocus
Jamaica ebony
Brown or green ebony

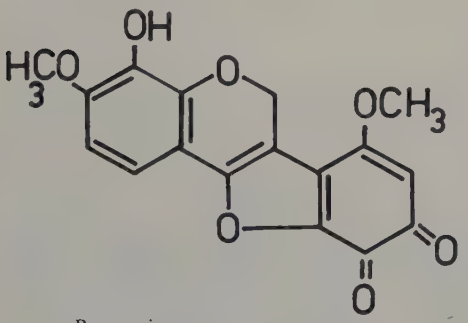
Small tree from the West Indies, especially from Jamaica and Cuba. Heartwood rich brown with a touch of olive colour when fresh; deepening to dark brown, beautifully veined. The decorative yellowish softwood is often used together with the heartwood. The small timber is hard, heavy and strong, of good stability (diameter usually not exceeding 7,5 - 15 cm).

Used specially for musical instruments, particularly for flutes, recorders and clarinets. Furthermore for interior turnery, cutlery handles and fancy articles as well as furniture (sawn veneers).

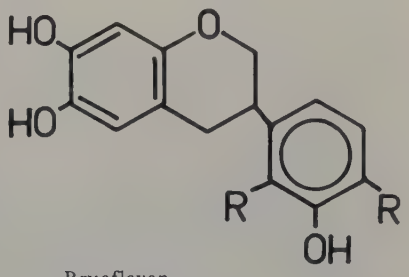
Since the beginning of the twentieth-century it has been known that Cocus causes irritation and allergic contact dermatitis in flute-makers sawing and sandpapering the wood, as well as allergic lesions of the lips and mouth in players from flutes made of this wood (Crocker 1903, Legge 1907, Meister 1934, Rockstro 1928, Schröpl 1934, White 1903).

Our sensitisation experiments in guinea pigs using the open epicutaneous method (see p. 29) were successful. Chemical investigation of the wood extract yielded at least five quinones, of which three could be isolated and later identified structurally by Ferreira & Thomson (1974, 1975) (bryaquinone). Another constituent - bryaflavan- is oxidisable over the diphenylmethylene ether with Fremy's salt to give an orange quinone. The flavanoid compound bryebinal oxidises at room temperature to an orange quinone.

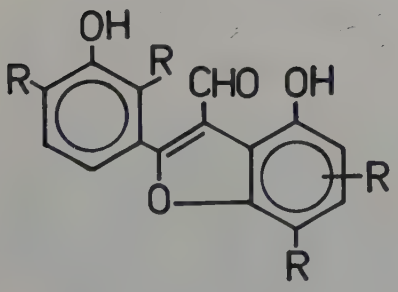
A further still unidentified quinonoid constituent running with a higher R_F-value on thin-layer-plates, gave the strongest allergic reactions in the sensitised guinea pigs (unpublished results).



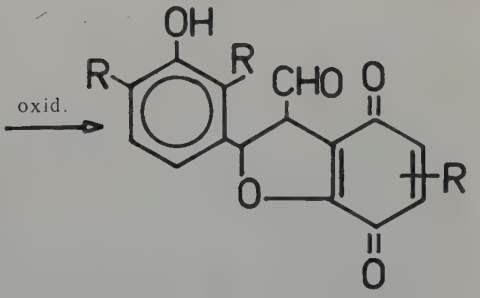
Bryaquinone



Bryaflavan



Bryebinal



Orange quinone

$R = OCH_3$

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Cordia millenii Baker
Cordia gerascanthus P.Br.
Cordia goeldiana Huber
(Boraginaceae)

Cordia, West African
Canalete (S-America)
Freijo, Frei jorge (S-America)

Cordia goeldiana from Brazil has been called Brazilian walnut occasionally and therefore caused confusion sometimes with *Ocotea* and *Phoebe* species. *C. gerascanthus* derives from Venezuela. *C. millenii* and also *C. platythyrsa* Baker are from tropical Africa (Nigeria).

All timbers are golden to medium brown and of no great durability. Due to their light weight, softness and low strenth properties they are easy to work with and are used only for interior work, furniture and joinery. The Brazilian species are suitable for boat-building and interior construction work.

There is no written evidence for the fact that *Cordia* species have caused dermatitis. Grossmann (1920) mentioned a type of 'rosewood' as source of dermatitis which he believed to be *Cordia alliodora (= C. gerascanthus)*. Schwartz (1931) described eleven cases of dermatitis due to 'Brazilian walnut', but it is not possible to establish if this was not in fact *Phoebe porosa* Mez.

Our own studies revealed that sensitisation of guinea pigs with extracts of *Cordia abyssinica* R.Br. as well as with *C. millenii* were successful. Using the OET all animals became allergic. Positive reactions were elicited with concentrations of the pure compounds down to 0,1 %. The threshold of primary irritation was 1 %. Moir & Thomson (1972, 1973) isolated and identified seven quinones from our extracts, which were kindly supplied and elicited in the sensitised animals. The cordiachromes A, B, E and F gave strong positive reactions and thus must be regarded as the main sensitisers.

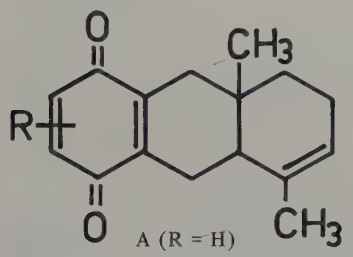
This new group of quinonoid constituents also occurs in *Patagonula* species (Moir & Thomson 1973).

Cordiachrome	24^h	48^h	72^h	identical with
Cordiachrome I	+++	++	-	cordiachrome A (yellow oil)
Cordiachrome II	+++	++	-	cordiachrome B (golden needles)
Cordiachrome III	+	+	-	-
Cordiachrome IV	++	++	-	cordiachrome E and F
Cordiachrome V	(+)	(+)	0	-
Cordiachrome VI	+	(+)	(+)	-
Cordiachrome VII	(+)	(+)	(+)	-

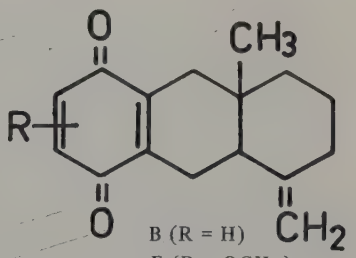
For evaluation of the reactions see p. 15; concentrations for patch tests: 0,1 %.

The next table reviews the *occurrence* of cordiachromes in different *Cordia* species (++ = high, + = low quantities) (Moir & Thomson 1973).

	Cordiachromes					
Species	A	B	C	D	E	F
Cordia abyssinica R.Br.	++	++	++	-	-	-
C. alliodora Ruiz & Pavon	++	++	++	-	-	-
C. gerascanthus P.Br.	++	++	++	-	-	-
C. goeldiana Huber	+	+	+	+	+	+
C. millenii Baker	++	++	++	+	+	+
C. platythyrsa Baker	++	++	++	+	+	+

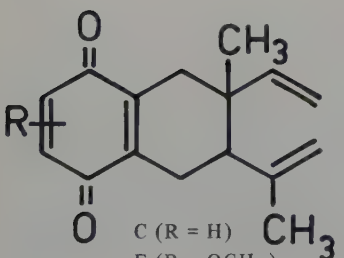


A (R = H)
D ($R = OCH_3$)

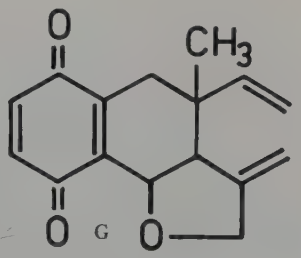


B (R = H)
E ($R = OCH_3$)

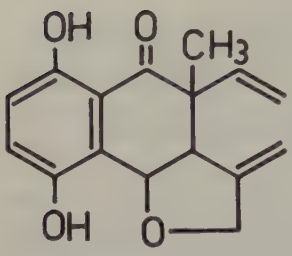
Cordiachromes



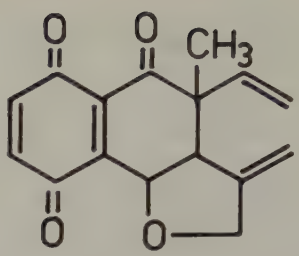
C (R = H)
F ($R = OCH_3$)



G



Leucocordiachrome H



Cordiachrome H

In *Patagonula americana* L. besides the cordiachromes already mentioned the two new compounds cordiachrome G and leucocordiachrome H have been found, the latter being oxidised to the new cordiachrome H (Moir & Thomson 1973).
Recently Manners et al. (1977) isolated six new geranyl-hydroquinone derivatives which allowed them to propose a detailed biogenetic pathway to the geranyl-benzoquinone constituents of *Cordia* species, as already proposed by Thomson some years before.

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Hymenea courbaril L.
(Legumin.- Caesalpin.)

Courbaril
Locust

Imported from tropical Central and South America (Amazon basin and Guyana) into England and West-Germany. A highly decorative timber of brown to violet colour, deepening to dark brown; hard, heavy and strong. Used for furniture, interior flooring and frames, turnery and boat-building.
Skin irritation has been described by Freise in 1932. Courbaril is included by Rasch (1925) in a list of poisonous woods. No definite description of the symptoms were given in these reports.
Thin-layer-chromatographic examination showed the presence of two different quinonoid compounds in the cold ethanol extract of the shavings. The constituent

with the higher R_F-value could be identified as 2,6-dimethoxy-1,4-benzoquinone (see p. 47). The other constituent has not been further investigated.
Reinvestigation of new wood samples in 1980 revealed the absence of the formerly obtained quinones. This may probably be due to the different origin of the wood samples (unpublished).

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Diospyros crassiflora Hiern.
(Ebenaceae)

Ebony, African
Ebenholz

Native to Nigeria, Cameroon and Gaboon. Usually marketed as short billets of heartwood (2 m long). Highly resistant to termites, of grey to black colour. Very hard to work with. Especially prized for its black colour for hard tool handles, pocket knives, door knobs, butt ends of billard cues, facing of tee squares, and table cutlery. African ebony is especially used for piano and organ keys, organ stops, violin finger boards and pegs, as well as parts of bagpipes.
Contact eczema has been described by Herxheimer (1912), Legge (1907) and Lewin (1928). Nicholas et al. (1935) reported a case of contact dermatitis following the wearing of an Ebony bracelet.
Allergic contact dermatitis is due to the naphthoquinones widely distributed among *Diospyros* species (see Ceylon ebony, Macassar).
Some *Diospyros* constituents with unknown but possible sensitising properties are listed in Table 6 (Tezuka et al. 1973). The occurrence of the quinonoid and related constituents is as follows:

1, 8	in: *Diospyros ferrea* (Willd.) Bakh. var. *buxifolia* (Rottb.) Bakh.
3	in: *D. japonica* Sieb. et Zucc. and in *D.kaki* L.fil. var. *sylvestris* Makino
2, 5, 7, 10	in: *Diospyros maritima* Blume
4, 6, 9	in: *Diospyros kaki* L.fil.

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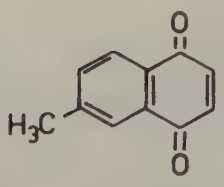
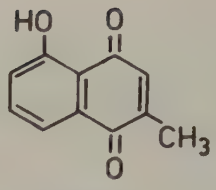
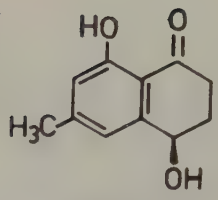


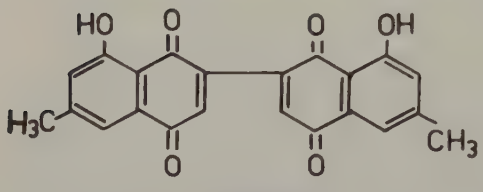
1 7-Methyljuglone



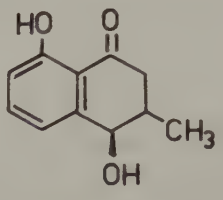
2 Plumbagin



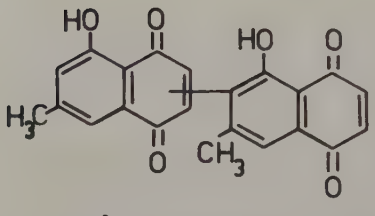
3 Shinanolone



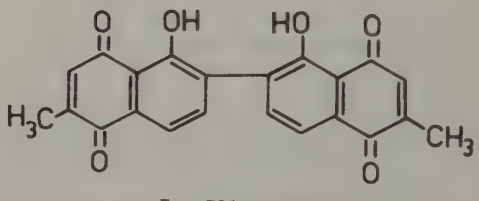
4 Manegakinone



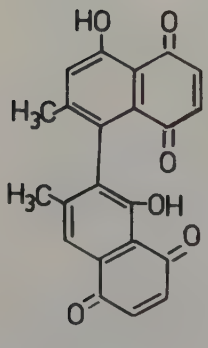
5 Isoshinanolone



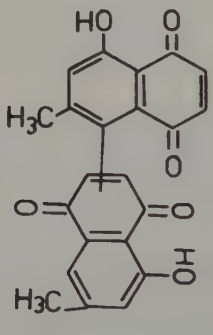
6 Diospyrin



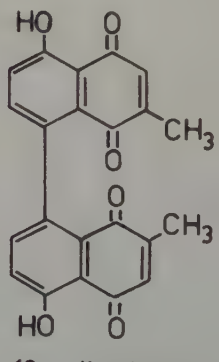
7 Elliptinone



8 Isodiospyrin



9 Neodiospyrin



10 Maritinone

Table 6 Quinonoid and related constituents of *Diospyros* species with unknown but possibly sensitising properties

Diospyros ebenum Koenig
(Ebenaceae)

Ebony, Ceylon
East Indian ebony

Imported in small boles from India, Sri Lanka, Celebes and Andaman Islands; of black colour. Strong, hard and heavy. Used for fingerboards, saddles, pegs, buttons and tailpieces of musical instruments, also for bow nuts and chinrests. Has good turnery properties and is also used for inlaying in cabinet working, for cutlery hafts, pocket knives, handles, brush backs, fancy ware. Eczematous reactions of the skin have been described after contact with the sawdust by Herxheimer (1912), Rasch (1925) and Reinl (1965). Grossmann reported a case of very severe irritation of the nose mucosa produced by sawdust put into the snuff of a worker for joke.
As causative agents quinones have been identified, but particular investigations on Ceylon ebony have not yet been made.
Other Ebony species such as Coromandel (*Diospyros melanoxylon* Roxb.), Persimmon (*Diospyros virginiana* L.) and *D. chloroxylon* Roxb. have been suspected for causing contact dermatitis. They contain some new quinones and biquinones of the type shown in Table 6 (p. 66). Some of these quinones have been proved to cross-react in guinea pigs sensitised with Macassar quinone obtained by oxidation of macassar II, a constituent of *Diospyros celebica* Bakh. (see Macassar).
Bleumink (1974) saw four positive patch tests with Coromandel.

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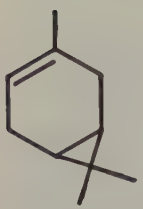
Pseudotsuga menziesii (Mirb.) Franco
(= ***Pseudotsuga douglasii*** Carr.)
(Pinaceae)

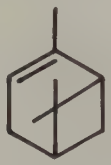
Fir, Douglas
Oregon pine
Douglasie

Native of the West Coast of North America, but also cultivated in Europe. Used for interior and exterior construction purposes, flooring, boat-building, door frames, veneer, furniture. Contains resins in its canals and an aromatic odour.
In a screening test 82 lumberworkers in British Columbia with contact eczema were patch-tested by Suskind (1967) with acetone and ethyl acetate extracts of Douglas fir. In two cases an allergy could be established. The patients did not react to turpentine. Nordin (1947) states that splinter wounds caused by Douglas fir are said to heal slowly and often become septic.
Suskind was successful with his extracts in sensitising guinea pigs. Though the causa-

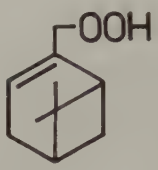
tive agents of Fir dermatitis are not known, it may be suggested the the resins, which contain the terpenes α-pinene, thunbergol and Δ^3-carene (0,6 %) may play a role as sensitisers (Erdtman 1968, Hancock 1965).
The *hydroperoxides* of these terpenes are known to be strong sensitising agents (Hellerström 1955, Pirilä 1966). Earlier cases were mentioned by Chittenden (1931) and Kämmerer (1956). A strong positive patch test with Oregon pine and negative results with several other woods were observed in a patient by Woods & Calnan (1976).

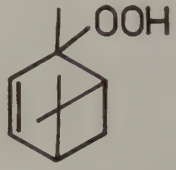


Δ^3-Carene



α-Pinene





Hydroperoxides of α-pinene

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Abies grandis L. — ***Fir***, Grand
Abies alba Mill. — White fir
Abies balsamea (L.) Mill — Silver fir, Balsam fir
(Pinaceae)

Abies alba grows in middle and southeast Europe. *Abies grandis* and *Abies balsamea* are native to USA and Canada. Usage is similar to that of other pines and spruces, e.g. interior construction work, joinery, plywood etc.
As early as 1887 White mentioned that the resins of these trees caused redness, itching, papules and eczematous eruptions when applied to the skin. Bonnevie (1939) saw recurring dermatitis of the hands after contact with Silver fir. He made sure that the dermatitis was due to the balsam by positive reactions to balsam and turpentine,

especially to α- and ß-pinene, but negative to colophony. In a second case a carpenter showed an isolated pinene-allergy.
Eczema of the hands and arms, later spreading to the neck and face, was observed by Ganzoni (1929) in a farmer, which always recurred in winter, when he felled and sawed Silver fir. Epicutaneous tests with the resins were strongly positive. A second farmer had the same etiologically established 'winter-eczema'. Kappes (1948) described balsam as a cause of contact dermatitis in a florist, who gave positive tests with Canada balsam (derived from *A. balsamea*). The patient was 'desensitised' by daily oral doses of up to five drops of balsam oil in milk over several weeks. This treatment was started again in November before the next Christmas season - the rash did not appear.
Further cases have been reported by Hjorth (1965) (12 cases caused by 'Fir') and Siemens (1929).
It must be suggested that the terpenoid compounds, or perhaps their hydroperoxides, are involved in the induction of this allergy (see Douglas fir, p. 67).
Sensitisation experiments carried out by Opdyke (1974) in 25 volunteers with oil of *Abies alba* using the human maximisation test failed.

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Aucoumea klaineana Pierre — ***Gaboon***
(Burseraceae) — Okumé

Imported from Gaboon, Guinea and the People's Republic of Congo in large quantities. A typical plywood and blockboard timber. Veneered plywood is used for panelling, doors etc. The solid timber is suitable for cigar boxes, packing cases and interior frame constructions. Logs are sliced on the quarter to give a semi-decorative veneer.
Dermatitis was described first by Spitzer in 1927, but he failed to establish the allergic conditions by patch tests on the patient. Subiza (1958) saw three cases of skin irritation but doubted their allergenic source.
Woods & Calnan described three attacks of dermatitis in a 53 year old joiner, manifested on the eyelids, backs of the hands and forearms. Epicutaneous tests were positive with Gaboon and Deal (Pine or Spruce). The responsible agents are not known.

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Entandophragma angolense C.DC
(Meliaceae)

Gedu nohor
Tiama
Edinam, Kalungi

Coming from West, Central and East Africa (Ivory Coast, Ghana, Nigeria, Zaire, Uganda) and exported to Europe a great deal. Resembling African mahogany, but lighter and plainer in appearance than Sapele and *Khaya ivorensis*.
Used as an alternative to Mahogany in the furniture industry, for boat-building, exterior and interior joinery, railway carriage constructions as well as for coffins.
Only two cases of contact dermatitis have been reported and described accurately by Schleicher in 1974. Several cases have been mentioned by Russian authors (Samigija 1972, Shevljakov 1974 - with five positive tests) and by Hublet (1972) and Oleffe (1973).
The allergenic constituents are unknown. Chemical investigations demonstrate a very low petroleum ether-soluble extract (0,1 %) (Adesida et al. 1967).

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Astronium fraxinifolium Schott.
(Anacardiaceae)

Gonçalo alves
Tigerwood
Zebrawood

Native of tropical America, especially Brazil. The heartwood is reddish-brown to dark red, hard, very decorative, only exported to Europe in small quantities. Used for furniture, flooring, joinery, veneers, arts and craft, resembles Rengas and Quebracho wood. The sawdust sometimes causes irritation of the skin which is so severe that the injuries resemble burns (Freise 1932). Though small quantities are exported constantly to Europe, no complaints have been published since 1932.

The relationship to other members of the Anacardiaceae family makes it probable that the phenolic vesicant and sensitising catechols of this family are possibly present also in this species. Thus a steady risk of skin eruptions may exist (see also chapter on Wood chemistry and Table 4, p. 24).

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Ocotea rodiaei Mez
(Lauraceae)

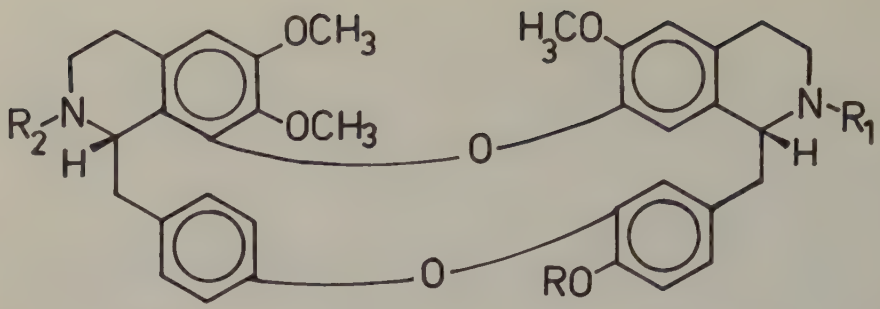
Greenheart
Demarara greenheart

Imported to Europe from Guyana and Surinam, very seldom from Brazil and Venezuela. Timber of light to dark olive-green colour which sometimes is marked with brown or black streaks, therefore also called sometimes Brown or Black greenheart. The wood possesses an extraordinary high strength and durability, is very heavy and hard, and has good resistance to marine borers.
In Europe used especially in harbours for piles, piers, lock gates, docks. In sawn form suitable for hand rails, handles of axes, flooring in factories, special engine parts. Occasionally used for fishing rods and longbows.
The sawdust is said to cause severe health injuries and irritation of the throat (Lewin 1928, Mackennis 1956, Vorreiter 1949). Splinters cause wounds which give trouble over a long period (Mackennis 1956).
As early as 1869/70 Maclagan isolated some alkaloids from the heartwood, which were said to develop a *curare-like* action (Anonymous 1940, Mackennis 1956). Seven greenheart alkaloids are known today (Hearst 1964, 1968). These constituents, which include members of the *bis*-benzylisoquinoline type, must be considered as the health hazards.
Many other South American species of the *Ocotea* and *Nectandra* genus are imported to Europe from Brazil and neighbour countries, most of them under the trade name of 'Louro' or 'Cane(l)la'. Some of these timbers, including African species, have been found to cause dermatitis or other hurtful symptoms (Piorkowski 1944, Schwartz 1948, Woods & Calnan), such as:

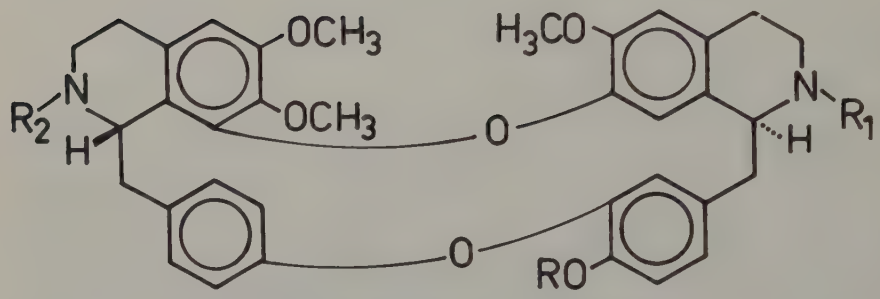
Ocotea barcellensis Mez	Louro inamni
Ocotea rubra Mez	Red Louro
Ocotea usambarensis Engl.	East African campherwood
Ocotea bullata E.Mey	Stinkwood

Woods saw five cases, two definite, three doubtful attributed to 'Louro'.

All these species contain alkaloids of the berberine and resperine-type. Known greenheart alkaloids are: demerarine, dirosine (most abundant = 11 %), norrodiasine, ocoteamine, ocodemerine, otocamine and rodiasine (Hearst 1964, 1968).



Ocoteamine = Sepeerine
$R = R_1 = H, R_2 = CH_3$



Demerarine

$R = R_1 = H, R_2 = CH_3$

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Grevillea robusta A.Cunn.
(Proteaceae)

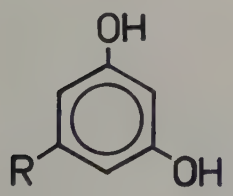
— ***Grevillea***
Australian silky-oak

A tree native to Australia, but planted also in Africa, India, Sri Lanka and other parts of the world.

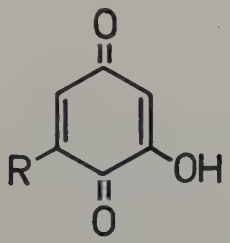
Suitable for plywood and furniture; a joinery wood of medium strength, gives average decorative veneer, used occasionally for flooring. Specially used in the United States and Australia as a shade tree on railways. Trees which have fallen during storms and must be cut by the workers of the (railway) telephone companies are said to cause 'Grevillea poisoning', because the sap develops erythema and bullae on the exposed areas of the body. The cases of dermatitis described seem to be of primary irritant origin, because strong bullous reactions always appear. Control persons have not been tested (Cleland 1925, Hurst 1942, May 1960, Morton 1971/1977). The flowers are said to be toxic too (Arnold 1944).

Chemical investigations of the wood revealed the presence of some phenolic compounds which are similar to those found in Poison ivy (Anacardiaceae) (see chapter on Wood chemistry, p. 21). The main constituent 'grevillol' (= 5-n-tridecylresorcinol) (93 % of the benzene extract) is easily oxidised *in vitro* to a *p*-quinone. Another phenolic constituent [5-(pentadec-10-enyl)-resorcinol] , which occurs in 1 % concentration in the wood, has vesicant properties (Occolowitz 1962 and personal communic.) (Ridley 1968, Ritchie 1965).

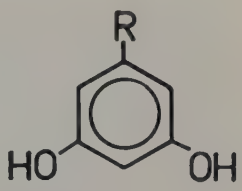
Although all catechol derivatives cause a primary irritation similar to the urushiols of the Anacardiaceae in high concentrations, they possess distinct sensitising properties. It is suggested that the Grevillea phenols exhibit similar properties.



Grevillol
$R = C_{13}H_{27}$



syn. Grevillea quinone
$R = C_{13}H_{27}$



5-(pentadec-10-enyl)-resorcinol
$R = C_{15}H_{27}$

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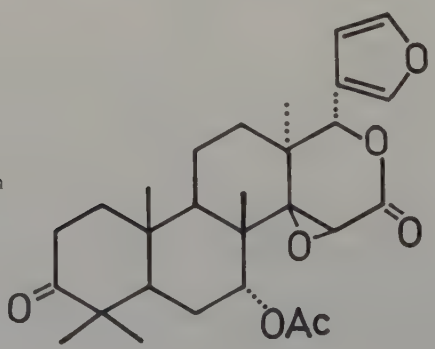
Guarea cedrata Pellegr. — ***Guarea***, White Bossé, Obobo

Guarea thompsonii Sprag. et Hutch. — ***Guarea***, Black
(Meliaceae)

Both timbers are marketed under the same trade name. Imports come from West Africa (Guinea, Senegal, Nigeria, Ivory Coast, Zaire).
The timber, of mahogany-type, is used for furniture, interior fittings, high-class joinery, underframes, tail boards, floor boards, sides of trucks and lorries, frames and planking in caravans. It exudes a resin which may be undesirable for certain purposes.

Though no clear descriptions of contact dermatitis have been published, several authors report severe irritations of the nose, throat and skin (see References). No patch tests and no intradermal injections have been performed to prove a possible allergic status. Farmer (1972) writes that the irritations of the skin, eyes, nose and respiratory tract are more marked with *Guarea thompsonii* than with *G. cedrata*.
Knowledge on the responsible constituents is lacking, but it may be said that the symptoms observed appear akin to a toxic or mechanically influence of the sawdust than to an allergic effect.
The heartwood of *Guarea thompsonii* contains several constituents which resemble the sensitising anthothecol of *Khaya anthotheca* (see Khaya), especially its constituent dihydrogedunin (Bevan 1963, Housley 1962).

Dihydrogedunin



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Liquidambar styraciflua L.
(Altingiaceae)

Gum, American sweet
Red gum, Bilsted
Amberbaum

Important timber of the United States (south east), Mexico and Central America. The heartwood is reddish-brown with a satiny lustre, attractive and with a fine texture. Only small quantities are exported to Europe, but in the United States Liquidambar is still a major timber. The wood is used widely for plywood, doors, boxes, furniture and joinery.

Cases of dermatitis have been described by Krais (1910) and mentioned by Grossmann (1920) and Legge (1907). Due to the frequent usage of the name 'Satin wood' in former years there may have been some confusion with other irritant Satinwoods such as *Fagara* species of the Rutaceae family. Nestler (1911, 1924) examined different extracts of the heartwood by applying them to his own skin. The ether extract produced a severe injury on his arm, which lasted for four months, leaving a scar. Though the wood is frequently used in the United States no further cases have been reported.

'Styrax' is a balsam deriving from *Liquidambar styraciflua* and *L.orientalis* trunks. Cases of styrax allergy have been noticed by Hjorth (1961) and Mitchell (1972). Patch tests gave two plus reactions with the balsam. The heartwood has been examined several times, but no compounds with properties hazardous to health have been reported. Own chemical studies gave no evidence for the occurrence of sensitising quinones.

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Eucalyptus saligna SM
(Myrtaceae)

Gum, Saligna
Sydney blue gum

Native to Australia, but planted together with other *Eucalyptus* species in South Africa and other countries. Heartwood pink to red. The plantation timbers are faster grown, lighter in weight and therefore usually lower in quality than the native Australian wood. Used widely for building constructions, flooring, packing cases, boxes, as mining timber and for pulp and fibreboard production.
A case of erythema multiforme-like eruption was described in 1976 by Holst et al. in a worker who had used the wood for two weeks in a workshop. The timber was probably *Eucalyptus saligna*. Patch tests with the wood dust produced a +++-reaction at 48 and 96 hour readings.

Our experiments with a sample of 500 g of the wood kindly supplied by the Timber Research and Development Association (TRADA) in High Wycombe, England, through the courtesy of Dr.Kirby, was extracted with ethanol and applied to the skin of guinea pigs, using the OET method at first and later the maximisation test (GPMT) (see p. 29). But the degree of sensitivity obtained was weak in both cases (unpubl. results).
A chemical investigation showed the presence of three quinonoid constituents, but they could not be isolated in sufficient amounts for tests on sensitised animals as insufficient wood was available. Based on TRADA information this wood is only brought to Europe very sporadically. Other *Eucalyptus* species are used in the woodworking industry of Australia and are also thought to cause dermatitis:

Eucalyptus maculata Hooker	Spotted gum	Baumer 1955 Morris 1943 Maiden 1909
Eucalyptus hemiphloia F.Mueller	Grey box, Grey gum	Maiden 1904 Cleland 1925

The latter is exported to England and used for the cross-arms of transmission and telegraph poles, underframing and decking of bridges. Oil of *Eucalyptus* trees may cause dermatitis too, poisoning after ingestion has been observed . Cases of *Eucalyptus* oil dermatitis have been reported due to the following species: *E.globulus* Labill., *E.microcorys* F.Mueller, *E.microtheca* F.Mueller, *E.regnans* F.Mueller, *E.tissilaris* F.Mueller (MacPherson 1923, 1925). Information on 17 cases of *Eucalyptus* oil poisoning have been reported by Witthauer (1922).

Woeber et al. (1969) established *Eucalyptus* oil-allergy by positive patch tests in sensitive patients.
Sensitisation experiments in 25 human volunteers carried out by Opdyke in 1975 using the *human* maximisation procedure and *Eucalyptus* oil derived from *E.globulus* and other species of the Myrtaceae family in 10 % concentrations failed to support the results of Woeber et al.

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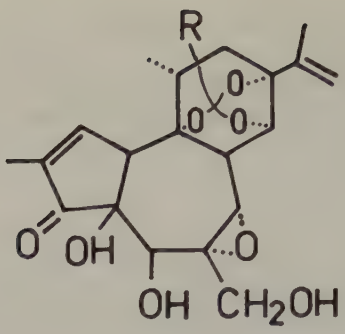
Hura crepitans L.
(Euphorbiaceae)

Hura
Sandbox tree, Assacu
Possentrie

Tropical beech tree of the West Indies and tropical America. The timber is used for interior joinery and constructions. In tropical America locally used for carpentry and furniture manufacture. The wood resembles Obeche. Imported only in small quantities. The sap of the tree - as true of all Euphorbiaceae timbers - has irritant properties and may cause blisters and inflammation of the face and eyes. Though several cases of irritation have been reported the wood is still exported and used (see References).
White stated as early as 1887 that it produced severe swelling of the face. In 1959 several cases of contact dermatitis occurred in a workshop where frames for exhibition jewellery boxes were manufactured from Hura (priv. comm. K.H.Schulz and H.Bellwinkel, Hamburg 1970). No patch tests were performed.
The latex of Hura contains some phorbol esters which are typical for Euphorbiaceae species and known for their strong primary irritant properties. One of these constituents has been isolated and named huratoxin. It is ten times as toxic to fish (and probably to man) as the known poison rotenone. An abrupt drop in toxicity results on removal of the side chain. This suggests that the long aliphatic side chain enables the molecule to penetrate easily into the cell (Sakata et al. 1971).



Huratoxin
$R = C_{13}H_{23}$

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Terminalia ivorensis A.Chev.
(Combretaceae)

Idigbo
Framiré, Emeri
Black Afara

Native to West Africa, especially Guinea, Ghana, Liberia and Cameroon. An attractive wood which sometimes contains brittleheart and occasionally may corrode metals due to its acidic properties. Suitable for joinery, furniture and interior and exterior construction purposes. Used also for flooring, but not recommended for kitchen equipment, because a yellow dye may stain fabrics in contact with the wood.
Though no case reports of dermatitis have been published, this wood is listed as irritant by Zafiropoulo et al. (1968). A weak positive test reaction has been obtained in a

Nigerian sawyer as mentioned by Woods & Calnan. Botanically near-related species are also said to be injurious to health: *Terminalia alata* Roth et spp. (Indian laurel) (Woods & Calnan) and *Terminalia chebula* Retz (Pilla murda) (Bernhard-Smith 1923). No alkaloids or quinones are present in the heartwood. Triterpenes have been isolated, but their physiological activities are still unknown (King et al. 1954, 1955).

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Ocotea porosa L.Barr.
(= ***Phoebe porosa*** Mez)
(Lauraceae)

Imbuya
Embuia, Imbuia

Only growing in Brazil. Heartwood often dark brown, but may vary from yellow olive to chocolate-brown. Developes a spicy resinous odour after cutting. Imported from Brazil mainly as logs and veneer. Used locally for high-grade furniture, interior joinery and flooring. Has good resistance against decay. Often falsely names Brazilian walnut. In Brazil the rootwood is particularly desired for highly decorative veneers. Seldom used for plywood manufacture.
Several authors have described the irritant properties of the sawdust (Mayers 1932, Mors 1961, Record 1929, Schmieg 1962). Schwartz (1931) saw eleven cases of dermatitis and obtained positive patch tests. Though there was some confusion about the identification of the wood, Record could show already in 1929 that the incriminated timber was in fact *Phoebe porosa*. Ordman noted in 1949 that some workmen developed contact dermatitis from Imbuya. According to Freise (1932) this wood contains two alkaloids which may cause cardiac stimulation, headache, vomiting and diarrhoea. Nothing is known about the skin irritating constituents of this species.

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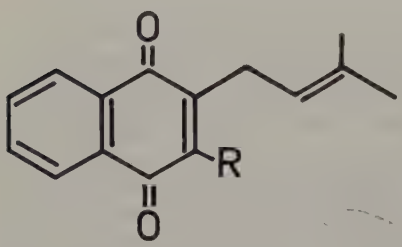
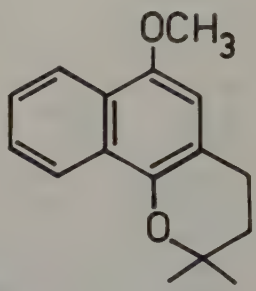
Tabebuia avellanedae Lor. ex Griseb.
(= ***Tabebuia ipé*** Standley)
(Bignoniaceae)

Ipé preto
Lapacho wood

This wood is of particular interest to its native countries Columbia, Venezuela, Brazil and Guyana: only few quantities are exported to Europe. It is suitable for interior and exterior work, joinery, handles, and used like Hickory. Together with other *Tabebuia* species Ipé preto is characterised by its high lapachol content (Burnett & Thomson 1967 = 3,5 %). Lapachol was first isolated from the heartwood in 1873 by Pekkolt, and later identified by Oesterle (1913, 1916).
Cases of dermatitis have been reported by Cordero et al. (1951) and were mentioned by Freise (1932) and Lewin (1928). Besides lapachol Casinovi et al. detected two further quinones in 1963 whereas Burnett & Thomson extended the series of quinonoid constituents in 1967 with seven further naphthoquinones and nine anthraquinones. Besides deoxylapachol, which must be considered as the main sensitiser of this species (Schulz et al. 1977) (yield: 9 mg from 500 g wood shavings) lapachenole (yield:68 mg from 500 g shavings) (Burnett & Thomson) may also play a role as sensitiser. Lapachol only functions as an elicitor.



Lapachol R = OH
Deoxylapachol R = H



Lapachenole

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Chlorophora excelsa Bentham & Hooker (Moraceae)

Iroko
Kambala, Mwule
Odum

Restricted in its occurrence to West Africa. Used frequently as a substitute for Teak because it possesses many of the desirable features of *Tectona grandis* L.

The first cases of dermatitis were described by Czimatis & Hagemann in 1910 in Germany. Since then more than 20 publications have appeared dealing with allergic contact dermatitis from Iroko. In 1949/50 King & Grundon isolated a hydroxystilbene - chlorophorin - from the wood, which later Schulz (1955, 1962) could show to be a sensitiser. He pointed out that this compound shows some structural relationship to the phenolic sensitisers of the Anacardiaceae family, considering the possibility that chlorophorin may be reductively cleaved to give two derivatives resembling urushiol or cardol equipped with unsaturated side chains.

Sensitising experiments in guinea pigs and preparative chemical studies carried out by Schmidt in 1963 with crude extracts of Iroko revealed that the amorphous chlorophorin could be separated into two different compounds, A and B. Only compound B was able to elicit strong allergic reactions in a sensitive patient. Sensitisation of guinea pigs in our laboratory was successful with an ethanol extract of the wood using the OET. Challenge with chlorophorin (20 %), isolated as an amorphous powder according to the method of King et al. from the same extract, gave positive test responses in the sensitised animals. The amorphous chlorophorin was then separated by two-dimensional preparative thin-layer chromatography into two different compounds C_1 and C_2. Both were used for eliciting skin reactions on sensitised guinea pigs.

	24^h	48^h	72^h
C_1	++	++	+
C_2	(+)	0	0

Skin reactions elicited by two different chlorophorin components in guinea pigs previously sensitised by a crude ethanol extract of *Chlorophora excelsa* (Iroko)

The results corroborated the findings of Schmidt (1963) and lead to the conclusion that crude chlorophorin is only a moderate sensitiser. However it consists of two compounds, of which only one is the real sensitiser, namely C_1. They are possibly isomers.

A related species in the Moraceae family is the so-called 'Fustic' *Chlorophora tinctoria* (L.) Gaudich ex Benth. & Hook.f., which contains the stilbene maclurin (see Table 3, p. 22), formerly used as a dye (Laidlaw 1959). Though this wood is listed as irritant too (Guns 1932, Pêche 1947), it is not known whether the tetrahydroxystilbene is responsible for this effect or not.

It is suggested that the hypothetic cleavage of chlorophorin into two compounds with unsaturated side chains is not the *only* possibility to become an effective sensitiser for chlorophorin could give rise to numerous quinonoid compounds on oxidation.

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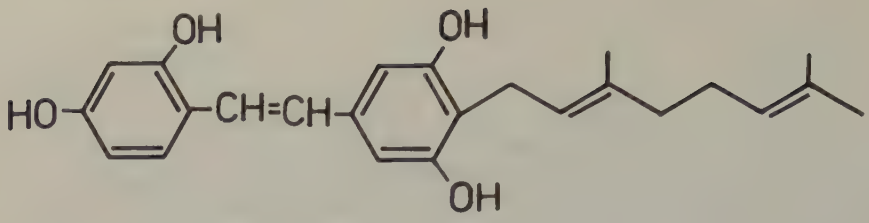

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Larix decidua Miller
Larix europaea DC
(Pinaceae)

Larch, European Lärche

This Middle-European wood is used widely for construction, frame-work, stairs, boat-building, flooring and construction of mills.
Only one case of contact urticaria from Larch recurring during manufacture of furniture has been described by Hanslian & Kadlec in 1964. Positive patch tests were ob-

tained with a petroleum ether extract of the veneer and an ether extract of the untreated wood. By chromatography the terpenes Δ^3-carene and α- and ß-pinene were shown to occur in the wood. Although the authors did not test these terpenes in the patient, they assumed that these substances could be the causative agents. Hydroperoxides of these terpenes are the source of turpentine allergy. In Fir dermatitis terpene hydroperoxides are suspected as the contact sensitisers (see p. 67-69), thus it may be suggested that in Larch dermatitis they may play a similar role. Woods & Calnan do not exclude the possibility that Larch dermatitis may be due to external lichens described by Schulman (1932) and Tenchio (1948) as causal agents in wood cutter's eczema (see Beech, p. 42).

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Shorea species
(Dipterocarpaceae)

Lauan, Red
White, Dark/Light Red, Yellow Meranti

Many species of the genus *Shorea* from south-East Asia provide timbers of commercial value which are called Lauan, Meranti or Seraya. According to their colour, specific gravity and botanical subdivision of the genus they are separated into four groups: White Meranti, Yellow Meranti, Light Red Meranti and Dark Meranti. Due to their attractive appearance, which sometimes resembles the mahogany-type, they are used for interior and exterior joinery, boat-building, flooring, furniture, plywood manufacture.

Skin irritations without detailed descriptions are mentioned by Hublet (1972), Oleffe (1973) and are known from verbal information. In a Meranti species, not identified more exactly than *Shorea sp.* we found the simple quinone 2,6-dimethoxy-1,4-benzoquinone. It may play a role as a skin irritant and sensitiser (Hausen 1978) (see p. 47).

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Terminalia superba Engler & Diels
(Combretaceae)

Limba
Afara, Korina (USA)

Native to West Africa from Guinea to Sierra Leone. 'Light Afara', a plain and light coloured wood is distinguished from 'Dark Afara', which is the figured heartwood. Usually of pale colour, this wood resembles Oak. Limba belongs to the five most important exported African timbers. The main importer is the Federal Republic of Germany, and 70 - 80 % is used in the West German veneer and plywood industry. Selected material sometimes has an attractive appearance and is therefore sliced to decorative veneer. Sawn wood is used for frames, table legs, chairs seats, drawer sides, coffins and interior joinery.
Though the timber is widely used in the wood industry skin irritations are rare. Sandermann & Barghoorn (1956) pointed out that splinters of Limba cause wounds and injuries which undergo increasing inflammation and resist healing. Vesicular eczema of the fingers due to Limba has been observed by Nordin (1947). Contact dermatitis was mentioned by Reinl (1965) and others (Anonymous 1950). Preissler (1959) reports bleeding of the nose and gum after exposure to Limba sawdust. A positive epicutaneous test has been obtained by Bleumink in 1974. Limba is considered to cause urticaria (verbal informations are known to the author). In some cases the 'rubbing test' gave positive results (see Clinical aspects, p. 8). However, most cases observed are respiratory disorders of the immediate type (see Chapter III).
Investigations of the wood in our laboratory gave no evidence for the occurrence of quinones or alkaloids nor for any sensitising capacity (unpublished results, 1974).

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Diospyros celebica Bakh.
(Ebenaceae)

Macassar ebony
Coromandel

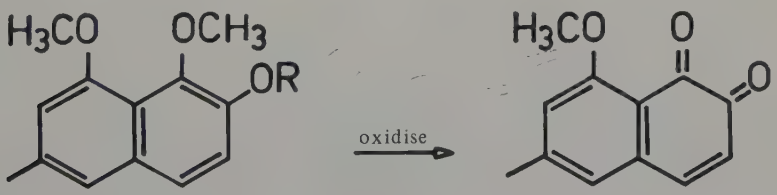
As the name indicates the tree comes from Celebes. Though ebony species of this origin are usually black, Macassar has characteristically light-coloured streaks which makes this strong and hard wood suitable for special decorative purposes such as cutlery hafts, knife-handles, brush backs and other small turned articles, inlay work in luxury furniture and boxes, rulers. A special use is for parts of musical instruments like fingerboards, saddles, pegs, bow nuts, tailpieces and buttons.

Dermatitis of the face, hands and forearms was described by Buschke & Joseph in 1927 in a 70 year old cabinet maker. The skin eruptions became generalised; other workmen at the same place were also effected. Patch tests with water and alcoholic extracts were negative, but an intradermal test provoked a positive response and was negative in controls. Another case was observed by Vonkennel (1929). A workman injured himself with an Ebony splinter. After healing he developed a squamous eczema shortly after renewed contact with Macassar sawdust. Though patch tests were not performed the author interpreted the skin lesions as an allergy. Schürkämper (1972) obtained a positive patch test to Macassar in one of 173 people in a veneer factory working with exotic timbers. Eaton (1973) states that in a British factory Macassar ebony caused so frequent problems that its use was discontinued and the wood had to be replaced by a 'Black ebony' species.

In 1957 Sandermann & Dietrichs isolated a main constituent of the wood, which they named macassar II and which seems to be responsible for the high termite resistance of this species. The structure was elucidated some years later by Brown & Thomson in 1965 who could show that this compound is easily oxidised to 8-methoxy-6-methyl-1,2-naphthoquinone, the deep red *Macassar quinone*, whereas another minor constituent - macassar III -, which is the methyl ether of macassar II is oxidised less easily to the yellow 5,6-dimethoxy-2-methyl-1,4-naphthoquinone.

Sensitisation experiments in guinea pigs performed with the pure Macassar quinone using the subcutaneous method had already shown in 1970 (I.Garbe, unpublished results) that one out of nine animals could be sensitised. A new attempt in 1974 to sensitise guinea pigs using the maximisation procedure (GPMT, see p. 31) was successful, revealing that all ten animals could be sensitised, giving positive reactions down to 1/100 molar dilutions (Buske 1974). These results revealed that, compared with other quinones such as thymoquinone, obtusaquinone or toluquinone, Macassar quinone is a moderate sensitiser (mean response = 1,88) (see Animal experiments, p. 31).

Further results were obtained by eliciting cross-reactions with four different naphthoquinones isolated from other *Diospyros* species (Fallas et al. 1968), named Q_1 - Q_4, in the guinea pigs sensitised with Macassar quinone. The strongest reactions were obtained with 2-methyl-5-methoxy-1,4-naphthoquinone, whereas 2-methyl-5,6-dimethoxy-1,4-nq., which is identical with the oxidation product of macassar III, mentioned above, remained negative (Buske 1974).

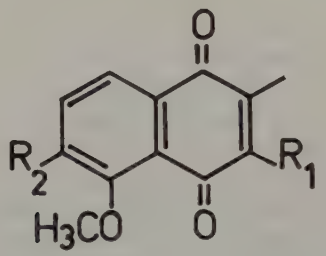


Macassar II R = H
Macassar III R = CH_3

Macassar quinone

Table 7 Comparison of the sensitising capacity of certain (mostly naturally occurring) quinones obtained by the maximisation test (GPMT, see p. 31)

Quinone	Occurrence		Mean response
Thymoquinone	Incense cedar	*Calocedrus decurrens* (Torr.) Florin	2.41
Obtusaquinone	Cocobolo	*Dalbergia retusa* Hemsl.	1.97
Macassar quinone	Macassar ebony	syn. from macassar II isolated from *Diospyros celebica* Bakh.	1.88
2,6-dimethoxy-1,4-benzoquinone	e.g. Makore	*Tieghemella heckelii* Pierre ex Chev.	1.61
Juglone	Walnut (shells)	*Juglans regia* L.	1.54
Toluquinone	Arthropodes	e.g. *Brachinus crepitans* L.	1.18
Lapachol	Teak	*Tectona grandis* L.	0.80
Rapanone	-	*Ardisia macrocarpa* Wall.	0.75
Quinone Q_4	Coromandel ebony	*Diospyros melanoxylon* Guill. & Perr.	0.40
2,5-dimethoxy-1,4-benzoquinone	Coromandel ebony	*Diospyros melanoxylon* Guill. & Perr.	0.00



Naphthoquinones from *Diospyros* species

Quinone				Mean response
Q_1	=	2-methyl-5-methoxy-1,4-naphthoquinone	$R_1 = R_2 = H$	0,55
Q_2	=	2-methyl-3-hydroxy-5-methoxy-1,4-nq.	$R_1 = OH, R_2 = H$	0,40
Q_3	=	2-methyl-5-methoxy-6-hydroxy-1,4-nq.	$R_1 = H, R_2 = OH$	0,10
Q_4	=	2-methyl-5,6-dimethoxy-1,4-naphthoquinone	$R_1 = H, R_2 = OCH_3$	0,00

24 hour reading, eliciting concentration: 1/20 molar

The results disclose that in all probability the Macassar quinone is responsible for the sensitising effect of Macassar ebony based on the hypothetical imagination that the main constituent of the wood, the phenolic precursor macassar II, is oxidised during the sensitisation process *in vivo* to the corresponding quinone. The other yellow quinone - 2-methyl-5,6-dimethoxy-1,4-naphthoquinone - obtained by oxidation of the

minor constituent macassar III seems to play no or only a secondary role. Finally, results showed that *o*-quinones do not differ in their sensitising capacity from that of *p*-quinones.

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Mahogany, African

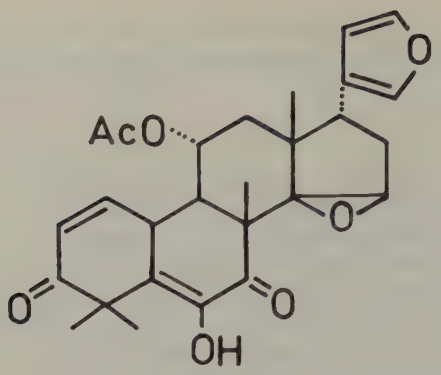
Khaya grandifolia DC	Big leaf mahogany
Khaya ivorensis A.Chev.	Khaya, Grand bassam mahogany
Khaya anthotheca C.DC	Krala, Acajou blanc
Khaya senegalensis A.Juss.	Dry zone mahogany

(Meliaceae)

The name for all species should be African mahogany as all four species are timbers of West Africa. Used for all purposes to which the real Mahogany was formerly suitable: furniture, cabinets, boat-building, in motor vehicles, vans and caravans for mouldings, interior parts of railway waggons, shelf divisions, office desks, etc.: generally all purposes where a good quality wood is required. The Mahogany timbers are mixed and not marketed separately and thus difficult to distinguish.

Outbreaks of dermatitis have been observed by Morgan et al. (1965, 1967, and 1968). Patch tests with the sawdust of all timbers used in the factory only gave positive respones with *Khaya anthotheca*. One of the allergenic constituents could be shown to be anthothecol, isolated by Bevan et al. in 1963, but the test reactions to this compound were only as strong as the wood dust itself. It thus must be considered that other sensitisers are suggested to occur in the wood.

By a simple chemical test it is possible to distinguish *Khaya anthotheca* from the other *Khaya* species: by staining a petroleum ether extract of the wood shavings with ferric chloride solution which will turn to red-brown when at least 0,03 % of anthothecol is present (Morgan 1967). Morgan described five further cases of dermatitis due to *Khaya anthotheca*, but he also saw a case caused by *Khaya ivorensis*, though this species does not contain anthothecol. This and further cases observed by Shevljakov in 1974 may support the assumption that other allergenic constituents have to be sought



Anthothecol

in *Khaya* species. One of these possible sensitisers may be 2,6-dimethoxy-1,4-benzoquinone which has been isolated and identified in *Khaya anthotheca* and *Khaya ivorensis* too (Hausen 1978) (see also p. 47).

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Swietenia macrophylla King

Swietenia mahagoni Jacq.
(Meliaceae)

Mahogany, American
Honduras mahogany
Tabasco, Caoba
West Indian, Spanish mahogany

In contrast to African mahogany these two species are generally known as American mahogany. This high-class wood, which has been considered for long time as the most valuable timber in the world, has been exploited so extensively from the 16th century until today, that most of the Mahogany resources have disappeared in South America. Today it is mostly replaced by African mahogany.
Reports of contact dermatitis have been communicated by Czimatis et al. in 1910 and later by Bonnevie (1939), Duke (1927), Frei (1931), Schwartz (1941), Steiner (1944), but only the cases of Schwartz and Steiner are really due to the American mahogany,

because the other authors did not identify the species. Two out of thirteen workers in a shipyard gave positive epicutaneous tests with the sawdust of Tabasco (Steiner et al. 1944). In recent years only two positive tests have been observed by independent authors (Hjorth 1979, Woods 1976). An allergic contact dermatitis was observed in a woodworker due to *Swietenia macrophylla* in May 1980 (priv.comm. Dr.Conde-Salazar, Madrid). After the species had been identified botanically and fractions had been prepared in our laboratory the patient refused to be tested epicutaneously.
There are chemical and botanical relationships between American and African mahogany examplified by the occurrence of their common constituent meliacin and its derivatives. They belong to the same chemical type as the sensitiser anthothecol (see p. 88) but it is not known if they possess sensitising power (Chowdhury; Das 1969). Our experiments with guinea pigs have shown that an ethanol extract of *Swietenia macrophylla* is able to induce sensitivity. By thin-layer chromatography 2,6-dimethoxy-1,4-benzoquinone was identified as a minor wood constituent (Hausen 1979; p.47).

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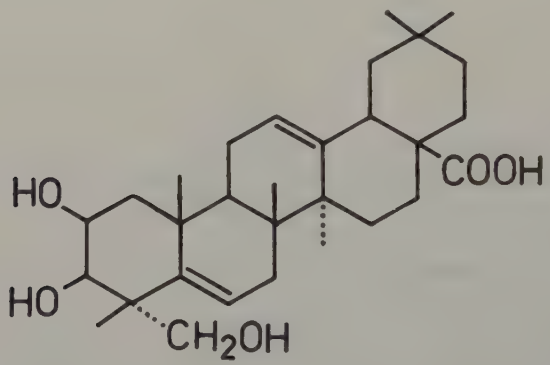
Tieghemella heckelii Pierre ex Chev. — ***Makoré***
(Sapotaceae) — Baku

A tree from West Africa that resembles Cherry wood in its colour or Mahogany. Therefore sometimes called African cherry or African mahogany. Used for furniture, veneer, high-class joinery, other decorative work, boat-building, coach panelling, planking, frames, doors, flooring for normal pedestrian traffic.
The wood is very well known for its irritating properties which are observed during sanding and machining (Farmer 1972). The dust irritates the mucous membranes of nose and throat, generally the whole respiratory tract. Dermatitis has also been communicated by several authors (see References). Khasabov (1977) obtained positive epicutaneous tests in 20 out of 179 woodworkers, but made no controls.

In 1959 Sandermann & Barghoorn isolated a saponin, the aglycone of which -bassic acid - was thought to be the irritating compound, but patch tests remained negative. Our investigations showed that in some cases not only primary irritant dermatitis but also allergic contact dermatitis may occur due to 2,6-dimethoxy-1,4-benzoquinone. This has been demonstrated in the following way:

A crude ethanol extract of the heartwood was used for the sensitisation of guinea pigs by the maximisation test (GPMT, see p. 31). After successful sensitisation (Makoré reveals only a weak sensitising capacity), different fractions were elicited on the sensitised animals, which had been obtained from the crude extract by chromatographic separation on preparative thin-layer plates. The second fraction contained the 2,6-dimethoxy-1,4-benzoquinone and elicitation experiments showed that only this fraction gave a positive skin reaction (Hausen 1978) (see also p. 47). Although 2,6-dimethoxy-1,4-benzoquinone has been detected in this wood the non-sensitising, - i.e. primary irritant effects of this species - are of more importance and hence the trade tends to discourage its use in the wood industry (Farmer 1972).

Similar irritant effects are seen with the sawdust of *Tieghemella africana* Pierre (Ukola, Douka) (Dahms 1955, Dantin-Galego 1952). Subiza Martin (1971) believes that the skin irritations are due to the histamine-liberating properties of the saponin mentioned above.



Bassic acid

a probably histamine-liberating substance from Makoré

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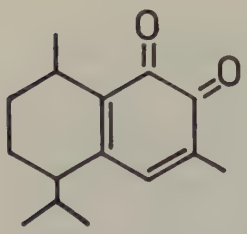
Mansonia altissima A.Chev. — ***Mansonia***
(Sterculiaceae) — Bété

This African timber grows in the Ivory coast. It is frequently used as a substitute for European or American walnut. Extremely resistant to termites. Suitable for cabinet work, radio and television sets, fancy turnery and joinery (billard cues) and similar purposes where Walnut is otherwise used.
The fine dust of the wood causes allergic contact dermatitis and besides that general symptoms like sneezing, nosebleeding, headache and cardial disturbances. Though it is troublesome to work with large quantities are imported into Western Europe. Exhaust ventilation is helpful, but sometimes very small quantities of sawdust may produce severe attacks when large amounts of the injurious constituents are present (personal experience). Allergic contact dermatitis has been described by at least 20 authors (see References). In Switzerland 400 pigs died due to severe skin lesions and other symptoms after being kept for some weeks on bedding of Mansonia wood shavings (Bertschinger 1970). Guinea pigs were sensitised by Schmidt (1963) with success.

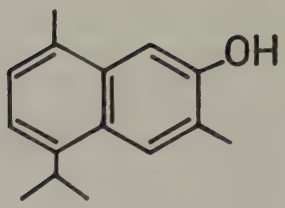
Chemical investigations disclosed the following correlations:

- ▲ Nosebleeding, headache, mucosal irritation and dizziness are due to a cardiac glycoside of the strophantin-type in the wood (see Table 4, p. 24/25)
- ▲ The allergenic conditions are produced by at least ten different quinones (called mansonones), the main component being the mansonone A
- ▲ Hanslian & Kadlec (1965) could prove that the severe skin irritations are further enlarged by unknown water-soluble components

The sesquiterpenoid quinones were first isolated by Sandermann & Dietrichs (1959) and tested epicutaneously by Schulz (1962), who could state their sensitising effect. Later on Marini-Bettolo et al. (1965, 1966), Galeffi et al. (1968, 1969) and Tanaka et al. (1966, 1967) extended the investigations and elucidated the structures of the quinones. It could be established that all mansonones - with one exception - are *o*-quinones. The main sensitiser mansonone A is easily obtained by steam distillation of the sawdust, but only when it is present. Mansonia samples from three different wood yards in Hamburg (West Germany) did not contain this quinone; however, a fourth sample yielded large amounts (1970).
Sensitisation experiments in guinea pigs demonstrated the strong sensitising property



Mansonone A



7-hydroxycadelene

of mansonone A (Schulz et al. 1979). With five of the ten known mansonones, kindly supplied by Prof.Tanaka, Tokyo, cross-reactions were elicited in guinea pigs sensitised with mansonone A. Though these quinones only occur in considerably lower amounts than mansonone A they may participate in the sensitising effects of this species.
It is interesting that the mansonones E and F occur in *Ulmus hollandica* Miller (Elm) which is resistant against Dutch elm disease. The fungitoxic mansonones are produced after infection with the fungus *Ceratocystis ulmi* (Buisman) C.Moreau (Overeem et al. 1970). Overeem et al. found the mansonones after inoculation of young branches and pointed out that it is reasonable to expect that the resistance of *U.hollandica* (and related species) is due to the fact that the produced mansonones show a striking similarity with the naturally occurring naphthols of these species, especially in *U.hollandica* with the 7-hydroxycadelene.

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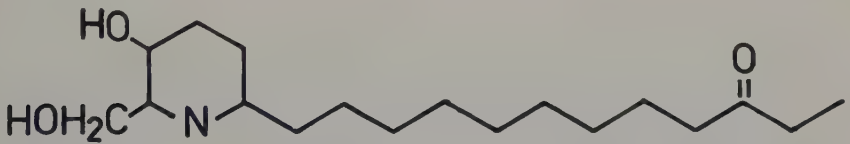
Prosopis juliflora DC — ***Mesquite***
(Legumin.- Mimosaceae)

This Central American timber is also cultivated in other countries. It is suitable for furniture, joinery and as interior and exterior construction wood.
Dermatitis of the face has been reported by Stewart in 1940 who obtained positive skin tests with the sawdust. Another case was observed by Fox (1941) in a farmer who used to burn Mesquite which he sawed up every day. Patch tests were positive with the moist sawdust and an ether extract. Cases have also been reported from India due to *Prosopis juliflora* and *P.specigera* L. (Behl et al. 1966). Shelmire (1940) has quoted two cases of health injury due to Prairie Mesquite = *Prosopis glandulosa* Torr.

Our thin-layer chromatographic investigation showed a spot giving positive colour reactions with a reagent for alkaloids, but this compound seems to be not identical with the *irritant* alkaloid prosopinine, isolated from the leaves of the closely related *Prosopis africana* Taub. by Bourrinet et al. in 1968. Mesquite and other *Prosopis* species are said to cause hay fever frequently in the United States (Iha et al. 1975, Novey 1977).



Prosopinine, irritant alkaloid of *Prosopis africana* leaves

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Pterocarpus angolensis DC
(Legumin.- Papilion.)

Muninga
Kejaat

A golden brown or chocolate brown timber of southern Central Africa, highly resistant to termites and of attractive appearance. Used for furniture, flooring, as veneer, for panelling and high-class joinery. There has been some confusion in the classification of the *Pterocarpus* species which generally are called Padauk.
Many complaints concern asthma (see Chapter III). An anonymous author (1957) suggested that the wood dust causes short breathing, coughing and gasping. Eaton (1973) saw an allergic contact dermatitis and obtained positive patch tets with the sawdust after 48 hours; the Padauk species was not identified botanically. Zafiropoulo (1968) mentions Muninga in his list of toxic woods. Padauk species are known to contain pterostilbenes, fungicidal constituents and various flavones (Bevan 1958, Morgan 1967). The nature of the compounds hazardous to health are not known.

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Triplochiton scleroxylon K.Schum.
(Sterculiaceae)

Obeche
Samba, Wawa
Abachi

A large tree from West Africa reaching a height of 45 - 55 meter. Colour white to pale straw, no clear distinction between heart- and sapwood. Widely used for all purposes for which durability and strength are not so important, suitable for plywood and veneers, as well as for interior rails, framing, joinery and model making, sometimes used for soundboards in organs. Imported into W-Germany and England in large quantities.

Most of the cases reported from Obeche are of asthma due to the fine sawdust (see Chapter III). Some rare cases of contact urticaria have been described by Oehling in 1963 and Gronemeyer in 1967. The urticarial conditions could be demonstrated by rubbing the skin with a chip of the wood giving an urticarial rash after some minutes. This 'rubbing test' result could not be reproduced in the patients by other woods or with Obeche in controls. Woods & Calnan mention a case of dermatitis from a lavatory seat manufactured from Obeche which was seen by Wilkinson who obtained a positive patch test.
Our studies have shown that neither alkaloids nor quinones are present in the wood.

With different extracts (ether, ethyl acetate, methanol) sensitisation experiments on guinea pigs using the open epicutaneous method (OET) failed (unpublished results). Chemical investigation of these extracts by Thomson revealed no compound which could be suspected as a health hazard (priv.comm., from Prof.Thomson, Aberdeen).

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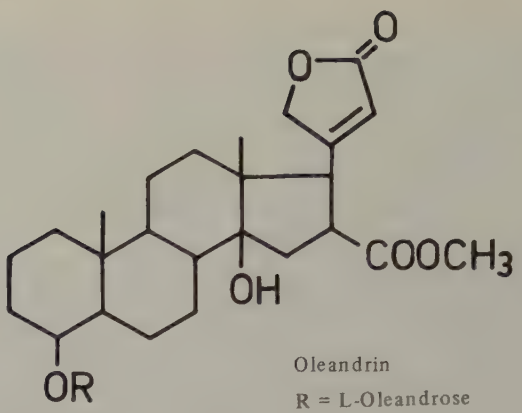
Nerium oleander L.
(Apocynaceae)

Oleander
Laurier-rose

Oleander is native to Asia and the Mediterranean region, and was introduced to most of the tropical and subtropical countries of Africa and America, where it is cultivated for the sake of its attractive red, pink and white flowers. This shrub is too small for the timber to be of commercial value but although its toxicity has long been known, accidental poisoning from the use of the wood continues to occur. The ingestion of one leaf may be lethal to human beings (Bors 1971) and animals (Szabuniewicz 1971). Accidental poisoning in humans occurred from chewing the flowers, eating meat cooked on Oleander branches or food stirred with Oleander stems (Szabuniewicz 1972). Whole families have been poisoned by using the branches as meat skewers , as mentioned by Allen (1943). Seven soldiers died in 1809 near Madrid after eating meat grilled on Oleander spits (Anonymous 1843, Wildeman 1948). Smoke derived from wood and leaves, and honey manufactured from the nectar of the Oleander blooms have been considered potentially dangerous to man (Arnold 1943). The toxicity of Oleander has been studied for more than 100 years in various animal experiments (Cornevin 1887, van Hasselt 1862, Pelikan 1866). From the United States there are reports of frequent poisoning following barbecues where Oleander spits cut by the Florida and California freeways were used (personal communication, Miami Hospital, Florida 1970). The active principles are oleandrin, neriine and other digitoxin-like glycosides. They are similar in physiological action to digitalis and have been used clinically, especially in Germany, Switzerland and France, in the treatment of human heart diseases as a substitute for digitalis (Szabuniewicz 1971).
The common *Nerium indicum* Miller, an evergreen shrub native to the southern slopes of the Himalayas, also contains dangerous amounts of poisonous glycosides. Extracts of the plant have been used in India in the treatment of leprosy, as an abortifacient and for suicides (Arnold 1944). Arnold mentions a case of a victim having eaten meat which was cooked over an open fire while spitted on a stick of Oleander wood.



Oleandrin
R = L-Oleandrose

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Olea europaea L. **Olive wood**
(Oleaceae)

Native to the Mediterranean countries, a small tree with fine texture, hard and heavy. Used for joinery and turnery, for handles, in Spain mostly for wooden jewellery such as necklaces, bracelets and napkin-rings and other fancy articles. Locally also for construction and firewood, occasionally for walking sticks. Used rarely in West Germany and Switzerland in the manufacture of high-quality recorders.
Irritation of the skin caused by Olive wood has been mentioned by Koelsch (1910), Legge (1907) and McCord (1958). A case of real Olive wood contact allergy has been communicated to us through the courtesy of Dr.Rothenborg from Copenhagen, Denmark. A 49 year old lady was in business as an importer of gift articles and fancy jewellery. Among these were bracelets and necklaces of Olive wood which she - walking around the department stores - demonstrated by wearing a few days every month.

Figure 9 Allergic contact dermatitis caused by a bracelet of Olivewood

she kept on wearing the bracelet - business before pleasure - when she went out to sell the jewellery to the large department stores. In the summer 1977 it was very hot in Denmark and the lady wore her necklace directly on the skin. A few days later she developed itching and dermatitis on the back of the neck and at the site of the bracelet (Figure 9). Patch tests were positive in the patient with scrapings of the bracelet, 31 controls remained negative. A thin-layer chromatographic separation of an ethanolic extract of the Olive wood in our laboratory yielded three Craven-positive (see p. 28) fractions which were sent to Copenhagen for testing. All three fractions gave a very strong response.

Sensitising experiments in guinea pigs with the extract revealed that all animals could be sensitised and further tests gave positive reactions down to 1 % dilutions. Eliciting with five separated Craven-positive newly prepared fractions gave strong positive reactions to the first three compounds and weaker to the others. Flare-up (see Immunological aspects, p. 13) was noticed at the site of the sensitisation area of the animals (Hausen et al. 1981). Further investigations and experiments are in progress.

Marweg (1968) found evidence for the occurrence of an alkaloid in the wood. A related timber *Olea hochstetteri* Baker from East Africa is used for furniture, panelling, turnery, vehicle building and tool handles (Farmer 1972). Skin irritations or dermatitis has not been reported.

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	Padauk (Padouk)
Pterocarpus soyauxii Taub.	Barwood, Camwood, Red African Padauk
Pterocarpus santalinus L.f.	Red sandalwood
Pterocarpus indicus Willd.	Amboyna
Pterocarpus dalbergioides Roxb.	Andaman Padauk, Vermilion wood (USA)

(Legumin.- Papilion.)

Besides *Pterocarpus soyauxii* which comes from Africa (Cameroon, Nigeria, Angola,, Zaire) all other Padauk species are natives of East Asia, the Andaman Islands, Indonesia, Thailand and the Philippines. Commonly the timbers are of attractive appearance, good strength properties, durability and stability. Suitable for joinery, turnery, boatbuilding, carving, handles, flooring. Used in the Eastern countries also for frames, construction of buildings and furniture.

As already mentioned with Muninga, the botanical identification and classification of Padauk species is confused. As early as 1910 Knebel stated that Padauk from the Sunda islands caused painful swelling and redness of the face. The two Padauk species he obtained, could not be identified botanically, but must be considered as *Pterocarpus santalinus* and *P.indicus*. Nestler (1927) investigated ethanol and ether extracts of a red Padauk species on his own skin, which caused irritation and itching. He regarded a red oil obtained from the wood as responsible for this reaction. The timber closely resembled *P.indicus*. A second Padauk wood of lighter colour produced no reactions. In 1957 sawmill workers in Hamburg (W-Germany) complained of an unpleasant and sweet taste in the mouth connected with repeated vomiting and irritation of the conjunctiva after contact with the dust of 'Ceylon mahogany'. The timber was identified as a *Pterocarpus* species, probably *P.santalinus* (Hausen 1970). The other Padauk species, named on the top of this page have also been suspected as health hazards (see References). All observed reactions must be considered as toxic and primary irritant reactions.

Pterocarpus species contain some fungicidal substances, flavones and a saponin (Morgan 1967, Bevan 1958, Simes 1959, Kumar 1974, Parthasarathy 1969). A chemical investigation of *P.soyauxii* which also causes irritation of the skin and mucosal membranes (Anonymous 1978) is in progress (W.C.Taylor,Sydney, personal comm. 1978).

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Aspidosperma peroba Fr.All. — ***Peroba rosa***
Aspidosperma vargasii A.DC — (Guatambu)
(Apocynaceae)

Both species are imported in large quantities from Brazil to Europe. Peroba rosa or Red peroba is rose-red and becomes brownish-yellow to medium brown on exposure. *A.vargasii* is somewhat lighter and often heartwood and sapwood are not distinguishable. The timbers are used for construction work and exterior joinery, turnery, furniture. In Brazil railway sleepers, boat-building, cabinets, brush backs, tool handles and toys are produced.

All wood species belonging to the Apocynaceae family are suspected to be toxic. The freshly cut wood, as well as the sawdust, causes general disturbances such as irritation of the nose, throat, eyes, coryza-like symptoms, weakness, cramps, sweating, drowsiness and faintness. Dermatitis and vesicular eruptions also have been observed (see References). Orsler (1969) has knowledge of some trade reports of skin and other effects from Peroba rosa on English workmen. The general symptoms are due to the occurrence of the pharmacologically highly active alkaloids of the quebrachine-type such as quebrachine, quebrachamine, physostigmine etc. (see Table 4, p. 24). They cause primary toxic skin irritations, accelerate breathing, visual disturbances, cardiac arrhythmia, but seem to produce no allergic reactions (Dixon & Ransom 1924).

An interesting new case has been observed recently by Brun (1978) in Geneva:

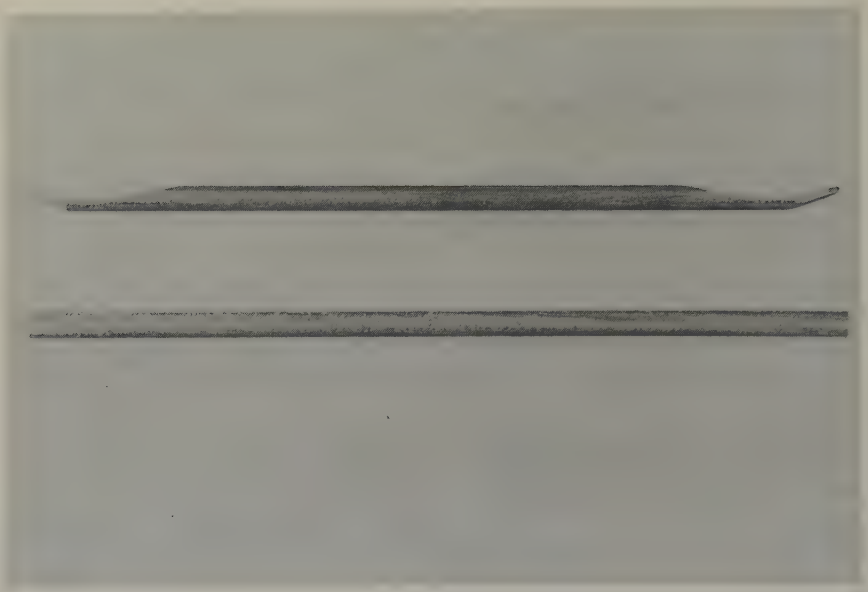
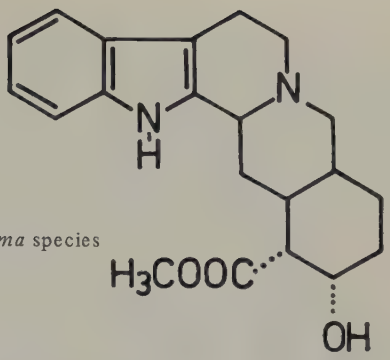


Figure 10 Cuticle stick of 'Orange wood' used for manicure (below: untreated piece of the imported *Aspidosperma* wood)

A young female manicurist developed eczema on her hands, localised in the interdigital spaces and the back of her right hand. The left hand only showed few areas of eczematous lesions, particularly at the base of the thumb. Epicutaneous tests using the standard series of the Geneva Dermatological Clinic remained negative. Further tests with twelve different products used at her working place such as varnish, lacquer, solvents, ointments etc. were negative too, and the keratolytic potassium hydroxide gave no reaction (pH 14). Tests with the wood of the cuticle stick were highly positive. It is a tradition among manicurists to use only so-called 'Orange wood' sticks and this wood has been identified by H.Gottwald (see Acknowledgements) to be Pau marfim *Aspidosperma sp.*

In all probability, none of the mentioned alkaloids of the quebrachine-type, can be made responsible for sensitisation. Chemical studies of the ethanol extract in our laboratory revealed no evidence for the occurrence of other constituents belonging to chemical classes of known sensitisers. Sensitisation experiments on guinea pigs revealed a strong sensitising capacity. Chemical studies to find the responsible contact allergens are in progress.



Quebrachine = Yohimbine
toxic alkaloid from *Aspidosperma* species

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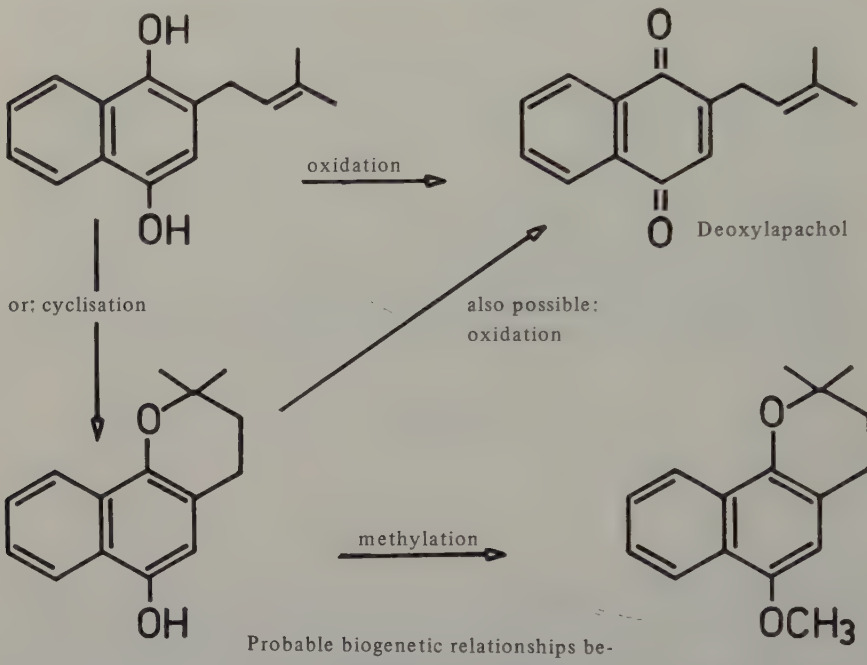
Paratecoma peroba Kuhlm.
(Bignoniaceae)

Peroba, White
Peroba dos campos
Peroba amarela, branca

This Brazilian wood of light olive or yellowish colour, sometimes striped, is used for frames, ship building, decking, flooring, and vats and tanks which are used with foodstuffs or chemicals. In its native country also used for good quality joinery and furniture. In former times it was used more extensively in Europe, but the quantities now imported are small.

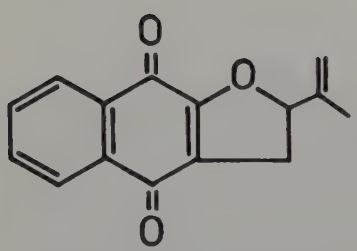
Some cases of dermatitis have been described by Barnett (1948) in England and mentioned by Farmer (1972). In 1951 five cases with positive patch tests to the sawdust and to lapachenole, an extractive from the wood, were observed by de Jong et al. Besides the main compound lapachenole, four quinones were isolated by Sandermann & Wendeborn in 1968, which have not been investigated for their sensitising capacity. They belong to the rare group of naturally occurring furano-quinones (see also acamelin on p. 47). Lapachenole is said to protect the wood from attacks by marine borers (*Teredo sp.*) and was investigated in a study on naphthoquinone sensitisation ca-

pacity by Schulz et al. (1977), showing that lapachenole reveals a strong sensitising power, nearly as effective as deoxylapachol (see also Teak). Biogenetically the two compounds are closely related, hence cross-reactions to deoxylapachol in guinea pigs sensitised with lapachenole are not surprising and have been obtained (Schulz 1977). It may be imagined that its activity may be owing to its conversion into deoxylapachol; alternatively deoxylapachol - the strong contact allergen of *Tectona grandis* L. - may function by cyclisation to lapachenole, as suggested here (Thomson, pers.comm.):

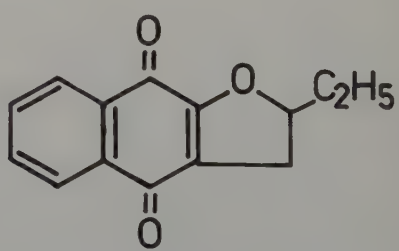


Probable biogenetic relationships between deoxylapachol and lapachenole

Lapachenole



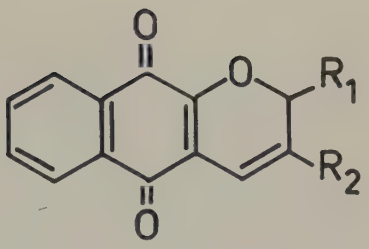
Dehydro-iso-α-lapachone



'α-Ethylfurano-1,4-naphthoquinone'

'ß-Methylpyrano-1,4-naphthoquinone'
$R_1 = CH_3, R_2 = H$

'ß-Hydroxy-α-methylpyrano-1,4-naphthoquinone'
$R_1 = OH, R_2 = CH_3$



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Pinus radiata D.Don
(= ***Pinus insignis*** Douglas ex Loudon)
(Pinaceae)

Pine, Radiata
Monterey pine

A native tree of southern California but cultivated in Chile, South Africa and Australia (since 1876). In Australia especially Radiata pine is used in the building industry, for box making and fancing, and for furniture manufacturing. The shavings and the sawdust are frequently used for packing flowers, for potting and for cleaning floors. Altogether 15 cases of allergic contact dermatitis due to Radiata pine have been described by Burry (1973, 1976, 1977). The patients gave positive reactions to the sawdust and in some cases also to colophony or to wood turpentine. These facts may support the suspicion that terpenoid components of the wood may be responsible for the allergy. Burry pointed out that the cases were discovered because colophony is used in adhesive plasters which caused contact dermatitis reactions when used in patch testing. Four out of the cases reported by Burry are of special interest, because sensitivity developed through different contacts with Radiata pine:

Case 1 woodworker, worked with Radiata pine as a hobby - positive to sawdust and colophony
Case 2 patient used Radiata pine for cleaning floors - positive to turpentine
Case 3 patient used sawdust for potting orchids
Case 4 gardener, used Radiata pine sawdust for packing flowers, suffered for 22 years.

Our sensitisation experiments in guinea pigs using the maximisation procedure (see p. 31) and an ethanol extract of the imported wood revealed only a relatively weak sensitising capacity.

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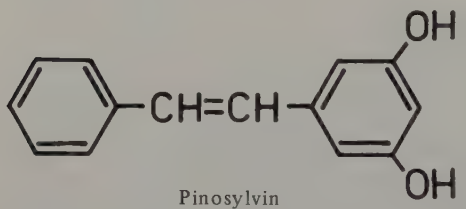
Pinus sylvestris L. — ***Pine***
Scots pine, Redwood, Red deal, Kiefer

Pinus pinaster Ait — Maritime pine
(= ***Pinus maritima*** Poir.)

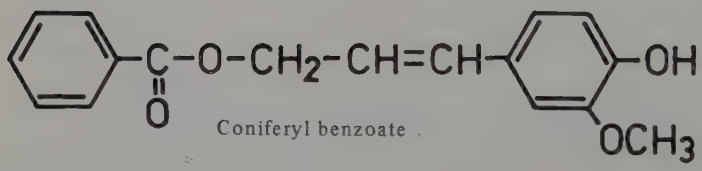
Pinus palustris Miller — Pitch pine
(Pinaceae)

Pinewood from northern Europe, the Mediterranean and North America is used all over the world for interior and exterior construction work, frames, stairs, railway sleepers, furniture etc. Dermatitis due to contact with Pine sawdust is well known (see References). Positive patch tests with the sawdust and extracts have been obtained by Beer (1970), Wilkinson (mentioned by Woods & Calnan); Jamieson (1933) reported six positive cases with 'Deal'. Irritation of the skin of the hands has been observed by Peri (1910) in workers treating iron pipes with shavings of Maritime pine. Erroneous suggestion concerning dermatitis due to Pitch pine (Cole & Driver 1928) arose from confusion over the name (Hausen 1970), but Bleumink et al. (1974) found positive patch tests in seven cases with authentic Pitch pine. Some curious cases of hypersensitivity to 'Christmas tree' extracts have been delt with by Szeyko in 1970 and mentioned by Ulrich (1965).
It is still unknown whether the sensitiser is pinosylvin, coniferyl benzoate, Δ^3-carene, other terpenoid constituents or their hydroperoxides (see Fir, p. 68) (Fregert 1963), (Hjorth 1961, Pirilä 1964).



Pinosylvin

Constituents of *Pinus* species suspected to play a role as sensitisers



Coniferyl benzoate

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	Poplar
Populus tremula L.	European aspen, Pappel
Populus alba L.	White poplar
Populus nigra L.	Black poplar
Populus balsamifera L.	Balsam poplar, Eastern cottonwood
Populus deltoides Marsh	American poplar

(Salicaceae)

The timbers are seldom marketed by species. Their quality may vary considerably according to the growing conditions. Most important are the home-grown poplars of France and Belgium. The timber is pale and of light weight. It is used for plywood, especially blind layers, but mainly for the manufacture of matches, chip baskets, etc. Also suitable for shelvings, interior joinery, toys and non-decorative turnery.

Weber described in 1935 some cases of allergic skin reactions in woodworkers after contact with the sawdust of Balsam poplar. Patch tests with the wet dust produced vesicular reactions. The dermatitis of the hands and forearms disappeared during absence from work but recurred on return under more severe conditions. A similar observation has been made by Caro (1953). Winkler (1956) treated two patients with contact dermatitis from White poplar resin. Epicutaneous tests the oil obtained by steam distillation of the resin, as well as with turpentine, were positive but negative on controls. The author suspected a situation similar to turpentine dermatitis and suggested that peroxides of α-pinene and Δ^3-carene might be involved as sensitisers (see p. 68). Dermatitis from Balm of Gilead derived from *Populus gileadensis* Roul. which in former times was a very common household remedy, was observed by White (1887) in several cases.

Dermatitis in bee-keepers arising from propolis is mostly connected with positive reactions to Poplar resin which is used by the bees as a glue in their bee hive. Thus there is a general belief, that the allergens in propolis are mainly derived from Poplar trees (Bunny 1968, Wanscher 1976).

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Gonystylus bancanus (Miq.) Baillon — ***Ramin***
(Thymelaeaceae) — Melawis

A small tree from south-east Asia (Java, Philippines), especially Sarawak and Borneo. It is not very durable and thus a subject to attack by termites. A substitute for Oak. Pale-coloured, lighter in weight than Beech. Used for furniture, toys, handles, mouldings, interior joinery. Imports increase steadily, especially to England and Germany. Farmer (1972) writes: 'it is reported that workers handling logs develop skin irritation'. Contact dermatitis has been observed by Wilkinson (cited by Woods & Calnan) with positive epicutaneous tests, and another case has been seen by Woods himself. A trade report of a rosacea-like skin irritation of the face was quoted by Hausen (1970). Other reports deal with positive intradermal tests with Ramin extracts without clinical symptoms (Oehling 1963).
Sensitisation experiments in guinea pigs have not been carried out but chemical investigations revealed the presence of 2,6-dimethoxy-1,4-benzoquinone in the wood (unpublished (see p. 47). Recently a new case of an itching rash spreading over the face, especially involving the eyelids, neck, shoulders and forearms, in a 41 year old wood machinist was reported by Beck (1980). Patch tests with wet and dry sawdust of Ramin were positive (++), similar responses were seen with wood tar. Controls remained negative. We propose to make a chemical reinvestigation of Ramin, supplied by Beck.

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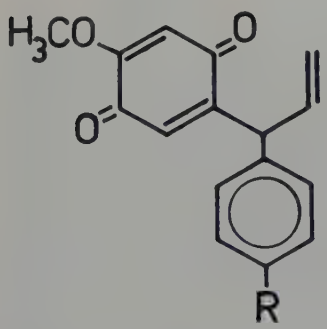
Dalbergia nigra All.
(Legumin.- Papilion.)

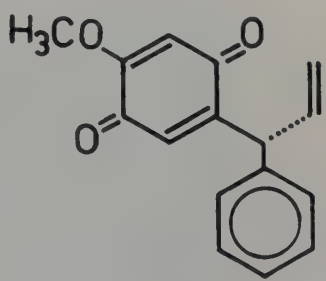
Rosewood, Brazilian
Jacarandá, Caviuna legítima
Rio-Palisander

A tree native to Brazil. The timber is only of attractive appearance when cut from old stems. Heartwood brown to chocolate, streaked with black. Imports are steady but low. Used for furniture and cabinets, handles, and especially musical instruments such as flutes, recorders, piano cases; gives an attractive decorative veneer. Very durable; in Brazil used for wooden jewellery, e.g. bracelets, necklaces etc. The wood of Caviuna vermelha (*Machaerium scleroxylum* Tul.) resembles Brazilian rosewood closely and is used frequently as a substitute (see Caviuna vermelha, Pao ferro, p. 51).

Since Gougerot et al. described the first case of eczema of the hands and face in 1922 at least 20 others have been published, arising from the wood dust and shavings produced in cabinet making or from direct contact with the wood itself (Escarte-Figue 1925), knife-handles (Hollander 1941, Hjorth 1961) or from playing of a Rosewood recorder (our observation 1979). Recent contributions have been given by Holst and by Woods & Calnan (ten patients) (1976). Cross-reactions to Rosewood were seen by Hjorth (1966) during patch testing of *Primula* sensitive patients. Similar observations were contributed by Krogh (1964) who found allergic reactions in seven workers sensitive to Teak, when tested with Rosewood dust. None of these persons had ever been exposed to Rosewood before.

The contact allergens of Brazilian rosewood have been identified by Eaton et al. between 1962 and 1965 as benzoquinones, called dalbergiones, whereas the sensitising power was established by Schulz & Dietrichs in 1962 and later by Schulz et al. (1979). Brazilian rosewood contains at least three dalbergiones which gave positive test responses in the cabinet makers tested by Schulz & Dietrichs. In animal experiments the dalbergiones showed a moderate to strong allergenic activity. Cross-reactions were obtained in the sensitised guinea pigs with primin, and with other dalbergiones, and were seen between three of the dalbergiones and deoxylapachol from Teak corroborating the test results of Hjorth and Krogh (see Figure 5, p. 20).





R-4-methoxydalbergione

S-4,4'-dimethoxydalbergione, R = OCH_3; S-4'-hydroxy-4-methoxydalbergione, R=OH

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Dalbergia latifolia Roxb.
(Legumin.-Papilion.)

Rosewood, East Indian
Ostindisch Palisander

In contrast to Brazilian rosewood this timber originates from India and Java. Its colour is purplish-brown with darker streaks terminating the growth zones. Gives a decorative veneer; is very durable and termite resistant. East Indian rosewood is used as for Brazilian rosewood, especially for high-class furniture and cabinet work, and frequently for parts of musical instruments and small turned articles such as flutes, recorders, guitars, chinrests, pegs, bridges of violins etc.

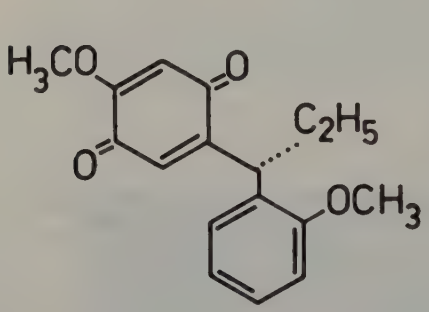
A case of contact dermatitis was first described by Stern in 1891 who observed a perioral eczema in a flute player. The wood was not identified clearly but was probably East Indian rosewood. Findlay (1972) reported a case of dermatitis due to indirect contact with the sawdust used for the manufacture of knife-handles. Cronin & Calnan (1975) saw a 60 year old butcher who presented a chronic eczema of the palms,which later spread to his forearms. Patch tests with shavings of a wooden knife-handle were positive. The wood was identified by the manufacturer as *D.latifolia*. After the butcher had been advised to stop using knives or other tools with wooden handles he made a satisfactory recovery. Two cases of allergic contact dermatitis in violin players were observed recently due to repeated contact with the chinrest made of East Indian rosewood. Patch tests were positive with shavings of the chinrest and the isolated quinones. In the first case (Hausen et al. 1979) only one quinone was positive, which did

Figure 11 a Chinrest made from East Indian rosewood *Dalbergia latifolia*

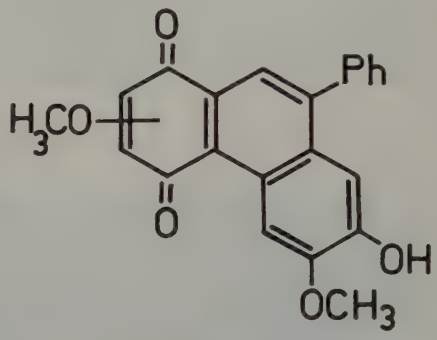
Figure 11 b Allergic skin lesions ('Fiddler's neck') due to extensive contact with a wooden chinrest

not belong to the dalbergiones (Figure 11 a,b). In the second case (Haustein 1981) R-3,4-dimethoxydalbergione, R- and S-4-methoxydalbergione, S-4,4'-dimethoxydalbergione and thymoquinone (see Cedar, p. 56) elicited positive skin responses (see References).

East Indian rosewood contains R- and S-4-methoxydalbergione, and the phenanthra-1,4-quinone latinone, isolated by Criodain et al. (1981), Donnelly et al. (1965,1968), Dempsey et al. (1963), Eyton et al. (1965) and Rao et al. (1963). Latinone resembles the sensitising cypripedin (7-hydroxy-2,8-dimethoxy-1,4-phenanthraquinone) recently isolated from the lady' slipper *Cypripedium calceolus* L. (Schmalle et al. 1979). The dihydro-2',4-dimethoxydalbergione, identified in 1967 by Donnelly et al. is probably identical with the 'yellow quinone' obtained by Kumari et al. in 1966. The sensitising capacity of the five dalbergiones was studied by Schulz et al. (1979) and revealed the following sequence of diminishing sensitising potency: R-3,4-dimethoxydalbergione >R- and S-4-methoxydalbergione > S-4,4'-dimethoxydalbergione >S-4'-hydroxy-4-methoxydalbergione (see also Brazilian rosewood, p. 107, Cocobolo, p. 58 and Caviuna vermelha, p. 51).



Dihydro-2',4-dimethoxydalbergione



Latinone Ph = Phenyl

Some other *Dalbergia* species are used commercially, e.g. for furniture, xylophone keys, turnery and parts of musical instruments. Most of them have been reported to be toxic or irritant, others are known to contain the sensitising dalbergiones:

Botanical name	Trade name	References
Dalbergia baroni Baker	Madagascar rosewood	Dietrichs 1971 Donnelly 1965/68
D.barretoana Hoehne	-	Silva Braga 1967
D.cochinchinensis Pierre	Siam rosewood	Dietrichs 1971 Donnelly 1968
D.inundata Bentham & Hooker	-	Leite de Almeida
D.lanceolaris L.	-	Lewin 1928

D.riparia (Mart.) Bentham	-	Braz Filho 1973
D.sisso Roxb.	Sisham	Dietrichs 1971
		Kulshresth 1974
D.spruceana (Vell.) Fr.All.	Para Jacarandá	Cook 1978
		Dietrichs 1971
D.stevensonii Standley	Honduras rosewood	Woods 1976
D.toxicaria Baillon	-	Lewin 1928
D.variabilis Vog.	Brazilian tulipwood	Kurasawa 1978
D.villosa Bentham	-	Silva Braga 1967
D.violacea (Vog.) Malme	-	Eyton 1965
		Gottlieb 1966
		Gregson 1978
		Ollis 1964

(Our investigation of a sample of *Dalbergia variabilis* gave no evidence for the occurrence of dalbergiones)

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Entandophragma cylindricum Sprague
(Meliaceae)

Sapele
Sapeli

A tree native to West Africa. A timber of mahogany-type, used as for African mahogany species (see p. 87) for furniture, joinery, mouldings, plywood, flooring, and as a decorative veneer.
Irritations of the skin have been mentioned by several authors (see References), but all reports were without convincing patch testing results. Two cases have been seen by Woods & Calnan with weakly positive test responses. The causative factors are unknown. Sensitising experiments are in progress.

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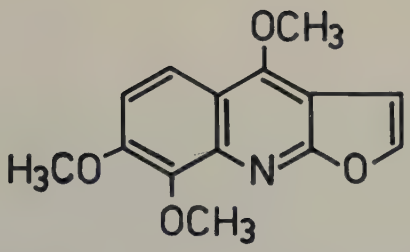
Chloroxylon swietenia DC
(Rutaceae)

Satinwood, Ceylon
East Indian satinwood

A tree native to India, and especially to Sri Lanka. The heartwood is light to golden yellow, darkening after some time to a soft brown colour. As it is remarkable lustrous its name is Satinwood. Owing to its decorative appearance it has been used for 80 years for cabinet work and interior furniture in ships. Generally used as a decorative veneer, but also for interior joinery and fancy goods.
The first report of contact dermatitis in cabinet makers in ship yards in England are from Jones (1904). As West Indian satinwood was also imported into England at that time there has been some confusion as to which of these timbers - East Indian or West Indian - was producing the toxic and irritant effects. Legge (1907) accused the East Indian wood whereas Bidie (1905) blamed the West Indian satinwood. There is also doubt in Gardiner's (1908) and Wechselmann's (1909) cases as to the causative species. Nestler (1924) performed some investigations on his own skin (with a sample of 'Satinwood'), but without success. The chemical investigation of Auld (1909) led to the isolation of the alkaloid skimmianine (see p.113), which was studied two years later by Cash (1911). The compound produced inflammation of the skin. Cash's study was one of the first experiments in the field of delayed-type hypersensitivity. At that time patch tests were uncommon and most of the authors were not familiar with that kind of experiment in human beings. The term 'allergy' had been introduced to medicine some five years before by von Pirquet (1906). The 'sensitising' effect of skimmi-



Skimmianine
Alkaloid of East Indian satinwood with blistering properties
(named Chloroxylonine by Auld 1909)

nine, which had been named chloroxylonine by Auld (1909), was not convincing, but Cash could not know at that time that alkaloids are not sensitisers,but at best histamine-liberating substances. Some 30 years later Mookerjee et al. (1946) showed that chloroxylonine is identical with skimmianine. It has blistering properties.Beyond this alkaloid East Indian satinwood contains some coumarins and furocoumarins with phototoxic properties (King 1954, Vrkoc 1972).
Our sensitising experiments in 15 guinea pigs using the OET (see p. 30) failed. Chemical investigation of the ether-, acetone- and ethanol extracts revealed neither a quinone nor any other compound which could be suspected as a sensitiser (unpublished). As no furhter cases have been reported since the publications of 1908 - 1911 it may be suggested that the former outbreaks of dermatitis were not allergic but rather phototoxic reactions produced by the furocoumarins and related compounds of the wood.

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Fagara flava Krug & Urban
(= ***Zanthoxylum flavum*** Vahl)
(Rutaceae)

Satinwood, West Indian
San Domingan satinwood

There is still disagreement between taxonomists and among phytochemists as to where to put this species - in the *Fagara* or *Zanthoxylum (Xanthoxylum)* genus. Other species with a lustrous appearance have also been named 'Satinwood' though they do not belong to either of these genera, but they are all described as toxic. Grows in the West Indies, Bermuda, the Bahamas and southern Florida. The timber is non-durable, but has a lustrous or golden yellow colour, darkening with exposure. Suitable for cabinet work, high-class furniture and interior decorative work, inlays, fancy goods and for turnery.

Satinwood dermatitis has been reported by several authors (see References). West Indian satinwood was also examined by Auld & Pickles in 1912 (see East Indian satinwood p. 112). They isolated two compounds believed to be lactones. Both were passed to Cash (1911) for further pharmacological studies but he never published his results so it must be supposed that the studies were without success. A later chemical study by Freise (1936) yielded an oily alkaloid which when tested on dogs and cats was found to be highly toxic. King et al. isolated in 1954 several coumarins of the psoralene type (see Table 4, p. 24) which are known for their phototoxic and photosensitising properties.

At least two other so-called Satinwoods have been held responsible for irritating effects: *Fagara macrophylla* Engler (African satinwood, Olongvogo) (Hausen 1970) and *Fagara heitzii* Aubr. & Pell. (Olon) (Pillon 1935, Woods 1976).

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Picea abies Karsten
(Pinaceae)

Spruce, European
(White wood), Fichte

One of the most used timbers of Europe, especially for constructions, telegraph poles, framework, flooring, boxes etc.
Most cases seen concerning Spruce are asthmatic (see Chpater III). Dermatitis is rare. Prosser White (1934) saw vesicles on the hands after cutting and sandpapering of Silver spruce (*P.sitchensis* Carr.). Fregert et al. (1963) reported cases of sensitivity to the balsams of Pine and Spruce. White (1917) mentioned 'poisoning' by Spruce. Bonnevie (1939) observed two cases of dermatitis with positive patch tests to turpentine, while Krüger (1924) mentioned an eczema caused by fresh construction wood, probably Spruce. Bleumink et al. (1974) obtained four positive patch tests with Spruce, Woods (1976) one. We have studied the case of a plumber engaged mainly in the fixing of gutters on new houses. For this purpose he had to saw and smooth Spruce planks (boards) on which he later fixed the gutters. He developed dermatitis of the face and neck recurring several times. One severe attack happended when he worked inside a vat, lined with Spruce planking. Ethanolic extracts of the wood gave strong positive reactions; Spanish turpentine oil also produced a positive skin response. Seven fractions obtained from the extract by thin-layer chromatography produced weak to strong reactions, one of them contained a Craven-positive compound (unpublished).
The turpentine obtained from Spruce is rich in terpenes, especially in Δ^3-carene. It is suggested that the hydroperoxides of these terpenes (Schantz et al. 1966) may play a role as sensitisers (see Fir, p. 68).

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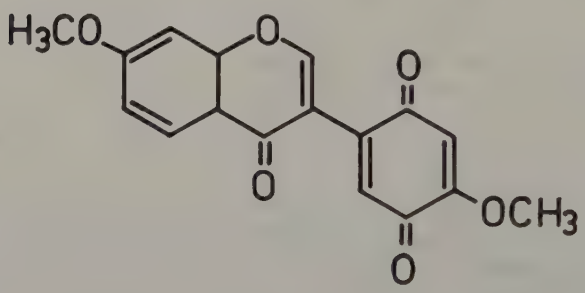
Bowdichia nitida Bentham
(Legumin.- Papilion.)

Sucupira

The name Sucupira or Sebipira is also used for the Brazilian species of *Diplotropis* and *Ferreira spectabilis* Fr.All. The heartwood is dark chocolate-brown with conspicous paler markings giving a decorative appearance. It is best suited for structural purposes

and mostly used in Europe for flooring. It is also of interest for turned articles and as a veneer for inlays in high-class furniture.

Cases of contact dermatitis have been mentioned by Freise (1932) and Dantin-Galego (1952). In 1966 Heyl described an allergic contact dermatitis in a joiner. Our investigations revealed the occurrence of three quinones in the wood which were isolated, purified and patch-tested in Heyl's patient. All three quinonoid fractions produced strong positive but different reactions. The first quinone was identified as 2,6-dimethoxy-1,4-benzoquinone (Hausen et al. 1972) (see also p. 47). The second quinone was found to be the first naturally occurring iso-flavonequinone (Brown et al. 1974). It was named bowdichione. The third quinone is still unknown but may be related to the dalbergiones, as the patient developed cross-reactions to R-3,4-dimethoxydalbergione and S-4'-hydroxy-4-methoxydalbergione (see Rosewoods, pp. 107, 108). Sensitising experiments in guinea pigs using the open epicutaneous method (OET, see. p. 30) were successful. A reinvestigation of Sucupira wood revealed the occurrence of at least five quinonoid constituents all of which gave positive reactions in the sensitised animals (unpublished).



Bowdichione
7-Hydroxy-3(5-methoxy-1,4-benzoquinone-2-yl)-chromone

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Tectona grandis L. ***Teak***
(Verbenaceae)

Teak comes from India, Burma, Thailand, Indo-China and Java, and has also been planted in Africa and the West Indies. The wood is brown and sometimes figured with dark streaks, Teak is strongly termite resistant. Like Lebanon cedar it is one of the oldest trade timbers of the world, and was used in Babylon and Egypt 4000 years ago. Used especially in ship building yards for decking, rails, bulwarks, hatches, weather doors owing to its good resistance to water which may be attributed to its high rubber content. Used also for interior fittings and mouldings, furniture, exterior joinery and flooring. Has a good resistance to chemicals and is therefore used for scrubbing towers, vats and fume ducts.

Teak has long been known for its 'toxic' properties. The first case of dermatitis was reported in a 'letter to the editor' in 'The Lancet' 1896 (Anonymous), while the first full description of a case of contact allergy was given by Evans (1905). Since that time more than 55 papers dealing with Teak allergy or its sensitising constituents have been published all over the world. The first chemical investigation was carried out by Matthes & Schreiber in 1914. Hoffmann (1926) was the first to declare that Teak dermatitis is due to a specific hypersensitivity against this wood. One of the possible sensitisers - lapachol - was found in 1959 by Sandermann & Dietrichs, but Schulz (1962) noticed during patch testing that there ought to be another - stronger - sensitiser in the wood. This second constituent - deoxylapachol (DOL) - was first discovered and identified by Sandermann & Simatupang (1962, 1963). Deoxylapachol differs from lapachol only by the absence of the hydroxy group at the third carbon atom of the quinone ring. Schulz (1962, 1967) demonstrated that this constituent was the *primary sensitiser*, giving 100 - 200 times stronger patch test reactions than lapachol. Outbreaks of allergic contact dermatitis in a furniture factory were studied by Krogh in 1962 and 1964. In seven out of 13 patients cross-reactions to Rosewood (probably Brazilian rosewood) were observed, although Rosewood had never been used in that factory. Fortyfour patients sensitive to Teak have been seen in recent years at St. John's Hospital in London (Woods & Calnan); most of the interesting cases dealing with Teak allergy are given in the References.

The content of the primary sensitiser - deoxylapachol - may vary so much in the heartwood that some samples contain none, whereas other samples from other sources may yield very large amounts. Plantation experiments carried out near Hamburg (W-Germany) showed that it is possible to grow Teak with containing little or no deoxylapachol. Teak grown in South Africa always contains very small amounts of the sensitiser (Dueholm 1970, Simatupang 1964).

Experimental studies on the sensitising capacity of DOL and lapachol in guinea pigs were made and published between 1970 and 1977 (Schulz et al. 1977). Using different method such as the open epicutaneous and subcutaneous sensitisation procedures (see p. 30) it could be demonstrated that DOL is a very strong sensitiser. By means of the same methods is was *not* possible to sensitise guinea pigs with lapachol; only cross reactions could be elicited with lapachol in DOL-sensitive guinea pigs. Lapachol thus

must be considered as elicitor or secondary allergen that may elicit reactions but is not able to induce specific hypersensitivity alone (for structure see p. 28, 80, 102). These results are in accordance with the hypothesis of Mayer, who suggested in 1928/1929 that only those benzo- and naphthoquinones which are able to conjugate with proteins of the body and thus complete to a full antigen are effective, i.e. quinones with an unsubstituted position in the quinonoid ring. (see also Chapter on Wood Chemistry, p. 21 - 29).

Cross-reactions obtained in animal experiments with DOL-sensitive guinea pigs and related quinones have been seen for example between DOL and primin (from *Primula obconica*), dalbergiones and mansonones. These results corroborate the findings of Krogh (1962, 1964) and Hjorth (1966) mentioned above in connection with Brazilian rosewood supporting the view that closely related quinones are able to elicit cross-reactions (see Figure 5, p. 20).

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Entandophragma utile Sprague (Meliaceae) — ***Utile***, Sipo

A West African timber of mahogany-type. Used as for Sapele and African mahogany, e.g. for furniture, cabinet work, interior and exterior joinery, constructions, frames, mouldings, fittings, decoratice veneer etc.
Irritations caused by the wood have been described in Nigerian workers (Woods 1976). A case of Utile dermatitis was reported from England (Woods & Calnan), another from East-Germany (Schleicher 1974). Further observations originate from Shevljakov (1969) from the Soviet Union. Bleumink (1974) obtained three positive patch tests in his patients. Sapele and Utile are used extensively, but their sensitising effects are low.
Sensitising experiments in guinea pigs were successful, but the mean response (see p. 31) remained low. A possible role may be played by 2,6-dimethoxy-1,4-benzoquinone, identified recently (Hausen 1978).

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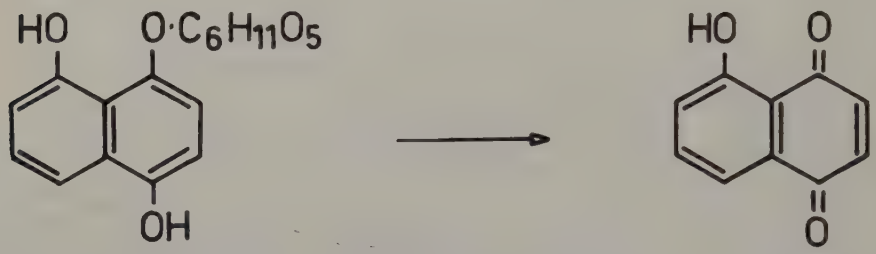
Juglans regia L. — ***Walnut***, European
Juglans nigra L. — ***Walnut***, Black
(Juglandaceae) — Walnuß

Though this tree is native to Europe, western and central Asia timber-producing trees of commercial value only grow in Italy, France, Yugoslavia and Turkey. Walnut trees are cultivated in north India and China. In the United States Black walnut is used. Walnut is one of the most desirable timbers for use as veneer, in cabinet making, furniture manufacture and decorative panelling; in solid form for high-quality furniture, fancy goods, gun and rifle stocks.
Case reports of dermatitis caused by both woods are rare and doubtful. The nut shells, only, of Walnut trees contain a simple naphthoquinone - juglone - which may be responsible for some cases of contact dermatitis of the hands contracted after handling the green shells reported by Barniske 1957) and Siegel (1954). Schürkämper (1972) in his screening tests of some hundred woodworkers found positive patch tests to European walnut in five persons, but these test responses occurred always in connection with simultaneous positive reactions to Teak and Cocobolo. Schleicher (1974) saw a case of contact eczema in a cabinet maker with positive tests to moist Walnut sawdust,

Controls were negative. He supposed that juglone was implicated based on his belief that this compound occurs in the wood. We examined a woodworker who developed slight dermatitis, itching and rhinitis after intensive contact with sawdust during the cutting of Walnut boards and the production of Walnut veneers. Epicutaneous tests with different wood species only gave a ++-reaction with Walnut and a weak reaction to Brazilian rosewood and Teak. The 'rubbing test' (see p. 8) with Walnut shavings produced a rash after 2 - 3 minutes. A chemical investigation of a Walnut ethanol extract led to a positive colour reaction with the Craven-test on analytical thin-layer plates (see p. 28). Further separation by preparative thin-layer chromatography yielded 4 mg of pure juglone from a total of 50 g wood shavings. This seems to be the first report of the isolation of juglone from the *heartwood* of a *Juglans* species. Patch tests with juglone in the patient gave a +-reaction to a 0,1 % concentration, whereas the toxic limit of juglone (threshold of primary skin irritation) had been determined before to lie between 1 % and 0,3 %. Seven controls remained negative. It may be concluded from these results that this patient had a slight hypersensitivity to juglone from Walnut. The itching complained by the patient previously may be explained by the highly primary irritant effect of juglone.



a-Hydrojuglone glucoside Juglone

Guinea pig sensitisation using the OET in ten Pirbright-white animals (see p. 30) was successful. All animals could be sensitised. The threshold of primary irritation of juglone was found between 0,3 and 1 % in the guinea pigs too. Eliciting with a 0,1 % dilution was positive in all animals, with a 0,03 % dilution still positive in two out of the ten sensitised guinea pigs. Cross-reactions were obtained in the sensitised animals with some other quinones, e.g. primin, deoxylapachol and R-3,4-dimethoxydalbergione (Halwass 1978). Conclusion: juglone is a strong irritant, a weak sensitiser and possibly a histamine liberator. Test concentrations should not exceed 0,1 % (see also p. 14,15). These results throw light on the findings of Schürkämper (mentioned above) who suggested that his positive test responses to *Juglans nigra*, which were always connected with simulatenous reactions to Teak and Cocobolo, may be based on the cross-reactivities existing between the naphthoquinones juglone and deoxylapachol, and the benzoquinonoid dalbergiones.

Juglone occurs in Walnut tissues as a glucoside of α-hydrojuglone (Daglish 1950). Hayes & Thomson (1955) could demonstrate that the naturally occurring α-hydrojuglone glucoside is the 4- and not the 5-glucoside.

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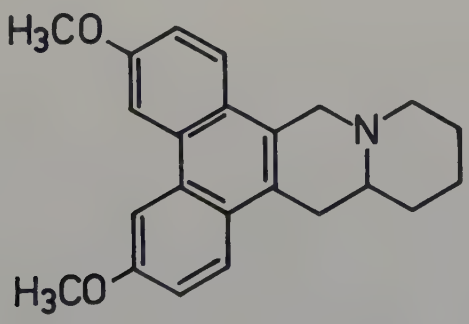
Cryptocarya pleurosperma White & Francis (Lauraceae) — ***Walnut, Poison***

Although the trade name points to its toxic properties Poison walnut is used a good deal in Australia as a construction wood, for stairs, mouldings and fittings , furniture, flooring and panelling, and as a veneer (Priv.comm. L.J.Webb and E.Gellert 1970). Sawing and cutting of the wood leads to painful dermatitis in cabinet workers and joiners two to three days after the first contact with the sawdust. Primarily the skin becomes red and blisters, and vesicles develop which then become squamous together with dry prutitus. The symptoms reach their maximum after two weeks and spread out to the face and scrotum together with headache and dizziness (Webb 1948). These symptoms could be reproduced by application of the alkaloid cryptopleurine, isolated from the heartwood by de La Lande (1948), to volunteers in concentrations of 0,1 %. The elucidation of the structure was made by Gellert et al. (1954, 1956).



Cryptopleurine

The alkaloid occurs in the bark, leaves and heartwood. Cryptopleurine also has been discovered in related *Cryptocarya* species and in *Boehmeria* species where it revealed its cytotoxic effect too (Hoffmann 1978). The primary irritant dermatitis produced by cryptopleurine is not based on an immunological mechanism, but arises from the histamine-liberating properties of the alkaloid.

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Millettia laurentii Wild. — ***Wengé***
Millettia stuhlmannii Taub. — Panga-panga
(Legumin.- Papilion.)

A tall tree from tropical West Africa (Cameroon to Zaire), especially from Zaire. There is no difference between the appearance and properties of both species. Heartwood dark brown with characteristic bands . Used as veneer and panelling on public buildings, hotels, show- and boardrooms, for flooring, general construction, interior and exterior joinery, high-class furniture, also in kitchens. Increasing in popularity - a timber with future.

Oleffe (1973), Hublet (1972) and others list Wengé and Panga-panga among other species as toxic, but give no details. The sawdust causes abdominal cramps (Hausen 1970) splinters of Wenge are said to cause persistent wounds. Bleumink (1974) obtained a positive patch test in a woodworker.

Sensitisation studies in guinea pigs using ethanol and choroform extracts were successful, and were repeated several times in different years. Both timbers showed the same sensitising capacity and chemical composition. Out of seven quinones detected five were isolated and tested on the sensitised guinea pigs giving positive reactions from weak to strong. The strongest patch test was obtained with a quinone of violet colour, contaminated by a Craven-negative compound which seemed to be inseparable from the quinone (unpublished results). One of the other quinones of yellow colour was 2,6-dimethoxy-1,4-benzoquinone (Hausen 1978). Though no definite case reports have been published these two wood species develop a considerable sensitising power in animal experiments, and therefore must be regarded as potent sensitisers of the future in the furniture and woodworking industries.

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Liriodendron tulipifera L.
(Magnoliaceae)

Whitewood, American
Tulip tree, Canary wood
Yellow wood

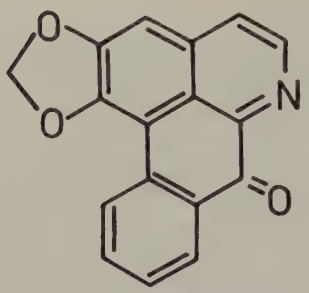
A tree native to the eastern United States. The heartwood is yellowish-brown or pale olive brown. Soft, light and easily worked. Used for interior parts of furniture, interior joinery, and many other purposes including plywood.

No description of cases in the literature despite two cases of dermatitis in a furniture factory in Hamburg (W-Germany) in 1912 (Brezina) due to 'Canary wood' which may have been Whitewood, and a mention of the toxicity of 'Tulipwood' due to the occurrence of an 'alkaloid' (Lewin 1928). Two cases of allergic contact dermatitis were recently observed by us on the hands, forearms, and neck and face due to American whitewood which occurred in a famous piano factory in northern Germany (Schulz et al. 1980). The wood had been used to make the cover of grand pianos. During debarking and cutting of the wood the two patients had contact with the moist wood dust and shavings.

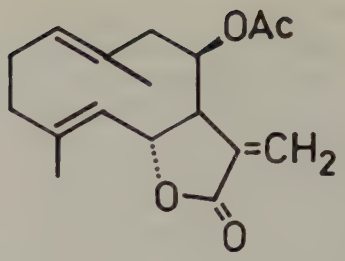
	A	B
Whitewood shavings	+++	(+)
Whitewood bark	-	++

While patient A reacted strongly to the wood itself and only weakly to the bark, patient B only gave a patch test response to the bark.

Chemical investigation of the bark and wood led to the isolation of different quinone-containing fractions, two of them giving a weak positive reaction on guinea pigs sensitised previously with a crude extract of the wood. One of the quinones was 2,6-dimethoxy-1,4-benzoquinone (see p. 47). Only fresh wood produced dermatitis, and quinones could only be detected in fresh wood and bark. The sensitising results using the maximisation procedure (see p. 30) indicate that Whitewood is a very weak sensitiser. There is some evidence that other constituents of the wood may play a more important role than these relatively ineffective quinones, for example the alkaloids (for primary irritant effects) and sesquiterpene lactones, which have been isolated in larger amounts (Abdusamatov 1974, Hufford 1975). Some of them occur in the roots and sapwood (Doskotch 1976, Senter 1977). Mitchell (1975) obtained positive patch tests in four out of five patients with the leaves of Whitewood, five controls remained negative. The leaves contain at least four sesquiterpene lactones which may have sensitising power: epitulipinolide, lipiferolide, peroxyferolide etc. (Doskotch 1969, 1970). Sesquiterpene lactones are well known for their sensitising capacity (Hausen 1979).



Liriodenine
(heartwood)



Epitulipinolide
(leaves)

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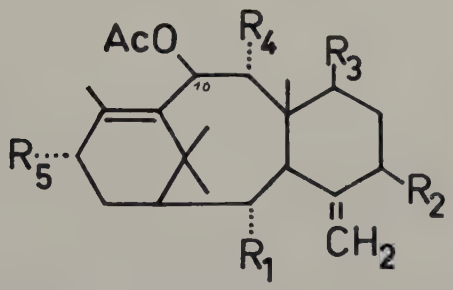
Taxus baccata L. — *Yew*
(Taxaceae) — Eibe

This small tree is native to Europe, Asia and North Africa. The heartwood is pale yellow to red brown, freshly cut with a violet lustre. A valuable wood for carving and turnery, sometimes used as a veneer, also for cabinet making, for arrows and bows. In certain countries the tree is protected.

The fine wood dust is said to produce irritation and dermatitis (Moll 1950). A case of severe dermatitis of the face, neck, hands and forearms has been described by Senear (1933) in a keen archer who carved a bow for himself in his leisure time. He patch tested himself with moist sawdust and got a response. Grossmann (1910) experienced headache and discomfort after working with Yew. The word toxic is based on *Taxus*. All symptoms observed support the suggestion that this wood is not able to induce an

allergy - they are toxic symptoms. The leaves, stems, bark, pollen and wood contain at least eleven different compounds called taxines, which are responsible for the toxic effects of Yew. They are terpenes (Baxter 1962, Harrison 1966). Some cause cardiac arrhythmia and decrease of blood pressure (Bauereis 1959). Higher doses produce cessation of respiration and death (Frohne 1965). Irritation of the skin may be due to an essential oil (Nicholson 1932). Poisoning of cattle and men by leaves of Yew is also well known (Frohen 1965, Powetz 1949,Czerwek 1960). Screening investigations of Yew heartwood with Dragendorf-reagent gave evidence for the occurrence of Dragendorf-positive constituents (0,03 %), which probably were a mixture of the taxines (Hausen 1970).



Heartwood constituents of *Tacus baccata* L.
(Harrison 1966, Della Casa de Marcano 1969)

Derivatives	R_1	R_2	R_3	R_4	R_5
I	H	OAc	H	OAc	OAc
II	H	OH	H	OAc	OH
III	OAc	OAc	H	OAc	OAc
IV	H	OAc	OAc	OAc	OAc
V	OAc	OAc	OAc	OAc	OAc
VI	M*	OAc	OAc	H	H
VII	M*	OH	OAc	OAc	H
VIII	M*	OAc	OAc	OAc	H
IX**	H	OH	H	OH	OH

* M = α-Methylbutyrate, ** OH at C-10

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III. Woods causing bronchial asthma and rhinitis

Fine dust particles are produced during woodworking processes like sawing, sanding, planing, turning, shaping etc. The mean particle size of the dust formed during the various operations ranges from 5 - 11 μm. 75 % of the dust samples have a diameter of 4,5 - 13,5 μm, but less than 25 % of the air-borne dust is less than 5μm. Studies of the concentration of dust in English factories showed that it ranged from 1-25 mg/m^3 with a medium at 5,9 mg/m^3 [11] .In an earlier study made in Czechoslovakia, Hanslian & Kadlec [10] determined an average dust concentration of 40 mg/m^3 with peak concentrations up to 200 mg/m^3. 90 % of the dust particles were less than 5 μm in diameter. These results indicate that in western Europe extract ventilation machines have become more modern and effective in recent years.

Inhalation of the fine dust particles may develop a composite picture of respiratory diseases with complaints of coughing, wheesing, dyspnoea, tightness, soreness of the chest, rhinitis and asthma [28]. It is doubtfull whether noticeable amounts of the wood dust particles are inhaled into the deeper parts of the respiratory system, i.e. into the alveolar regions and bronchi of the lungs; most of the material will effectively be trapped in the nasal passages on inhalation [11,27]. However, small amounts of the dust particles will finally pass down to the bronchi, where they may cause cramps and spasms in the tiny muscles of the bronchi. Therefore the correct name must be bronchial asthma.

Immunological aspects

Bronchial asthma may be caused by different factors, for example by unspecific irritants like an infection, chemical and physical hazards, or physical efforts and even emotions. *Allergic* bronchial asthma is always the consequence of an antigen-antibody-reaction due to the inhalation of a specific antigen, which comes into contact with the cell-bound antibodies in the bronchial tree, the nasal mucosa and the conjunctival tissues. Allergic bronchial asthma belongs to the type-I-reactions according to Gell & Coombs [9] (see Immunological aspects p. 10). The antibodies are immunoglobulins belonging mostly to the IgE-class. These IgE-antibodies may be detected in the serum and can be demonstrated by the ability of the patient's serum to passively sensitise the skin of normal humans or monkeys (Prausnitz-Küstner-test). The antigen reacts with this specific class of antibodies which are bound to the surface of mast cells or circulating basophils through a specialised region of their body, the Fc piece, while another part, the Fab fragment, remains free (Figure 12). The IgE-antibodies are fixed to the mast cells in the different tissues over a long period which becomes 'sensitised' in this way. Contact with inhaled or ingested specific antigens is followed by degranulation of the mast cells and release of different pharmacological active compounds - the vasoactive amines - which cause the typical clinical picture of an acute asthma attack:

- intense constriction of the bronchioles and bronchi (contraction of smooth muscle)
- dilatation of capillaries
- dyscrinism (perversion of the secretion of an endocrine gland)

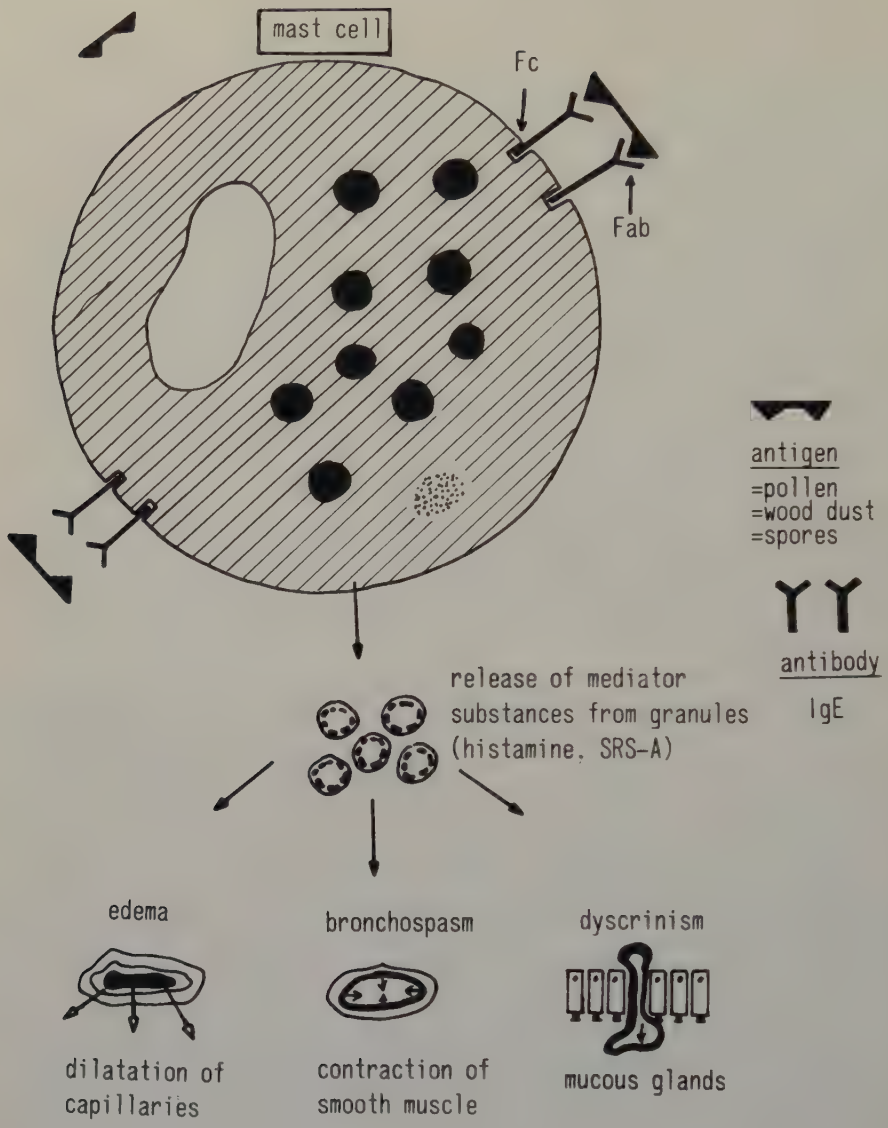


Figure 12 Allergy of the immediate type (type-I). Degranulation of mast cells following interaction of antigens with bound IgE-antibodies

These mediator substances are histamine, serotonin, SRS-A (slow reacting substance of anaphylaxis) and others [24]. The degranulation of the mast cells occurs when the bound antibodies are cross-linked either by specific antigens or by the corresponding divalent anti-immunoglobulin (anti-IgE) (Figure 12).

Attacks of bronchial asthma due to inhalation of wood dust last from a few minutes to several hours; they have been categorised as immediate, late and combined, i.e. dual asthmatic reactions. Generally, most patients are exposed to a variety of wood dusts for years before respiratory symptoms occur. After a period of steady exposure they begin to cough and become breathless. A few develop burning and running of the eyes as well as nasal obstructions or rhinorrhoea. In the early stages coughing occur only at night or in the late afternoon and is accompanied by little or no sputum. Relief may occur during the weekends, especially on Sundays. A single exposure in a sensitised subject may produce symptoms recurring for two or three nights. The final clinical picture is that of chronic asthma or bronchitis with evening or nocturnal exacerbations. By this time there is little obvious temporal relationship between exposure and the exacerbation of symptoms [18].

Allergic rhinitis and bronchial asthma are examined by scratch-test, intradermal test or prick-test with aqueous extracts of the sawdust of the offending wood species. Most frequently the intradermal test is used. In cases where this test remains negative an inhalative provocation test (bronchial challenge test) should be performed. All tests must be carried out with care, control tests are often necessary for the correct interprettation of the response obtained.

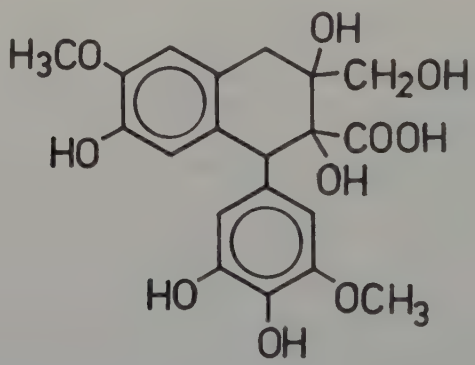
Occupational allergic rhinitis and bronchial asthma due to the inhalation of different wood dusts has been noticed and described all over the world [2]. According to the number of reports submitted to the Workmen Compensation Bureaux in Western Europe it seems that immediate hypersensitivity (type-I-allergy) due to wood dusts constitutes *one third* of all allergic diseases caused by commercial timbers (see also p. 4). A list of wood species causing allergic rhinitis and bronchial asthma is given in Table 8.

Intensive research has been carried out on bronchial asthma caused by exposure to Western red cedar *Thuja plicata* D.Don. This timber is one of the seven species of cedar growing in North America which are of substantial commercial value. Its good durability makes it suitable for outdoor and indoor constructions. Western red cedar has been exported from British Columbia and some States of the USA to Australia, Japan and other countries since 1960. It has found increasing favour in the joinery trade, especially in Australia [8,18]. Respiratory symptoms have been mentioned as early as in 1904 by Maiden [16]. Large amounts of Western red cedar were exported from Canada and the USA to Japan as a gift after the great earthquake in 1923. The wood was used mainly for rebuilding of the houses destroyed. Inhalation of the fine wood dust by Japanese joiners was soon followed by attacks of Western red cedar asthma called 'beisugi asthma'. Several cases were reported by Japanese authors [15,17,26]. Beisugi asthma was contracted even by people who never had contact with the wood dust or particles, but who lived in houses built of Western red cedar. The attacks were initiated by the constituents excreted by diffusion from the walls and ceilings of Western

red cedar [18]. According to Mue et al (1972, 1975) [21] about 9,5 % of all Japanese woodworkers engaged in house building today develop asthmatogenic symptoms after inhalation of imported Western red cedar sawdust. Similar conditions of bronchial asthma and rhinitis resulting from exposure to the related Japanese cedar species *Thuja standishii* Carr. have been described [14] and investigated by Ito (1963, 1964) [13].

Brief reports of asthma amongst men using Western red cedar in other countries have been made by Ordman in South Africa [3] and Doig in England [5]. The clinical picture was first described in detail by Milne et al. (1969) [18], Gandevia (1970) [8] and Mitchell (1970) in Australia [19] as well as by Chan-Yeung et al. (1972, 1973, 1976) in Canada [4], and by Ishizaki et al. (1973) in Japan [12]. They stated that asthma to Western red cedar is a typical dual asthmatic reaction. Chan-Yeung could show that skin testing with extracts of Western red cedar - as already stated by Milne in 1969 - is not helpful in diagnosis. Only inhalation provocation tests provide a reliable method of confirming the diagnosis. This test is carried out by an aerosol of the wood extract or of the suspected sensitising agent (e.g. plicatic acid) which is inhaled under controlled conditions to reproduce the symptoms and to obtain objective evidence of airway obstructions. Control tests - inhalation of the diluent or an extract of another wood - should be performed on the previous day to exclude any non-specific response [4].

Though it is a general belief that the causative agents in allergic bronchial asthma, i.e. type-I-allergy, due to plants and wood dusts are high molecular weight components, e. g. proteins, Chan-Yeung et al. demonstrated by their investigations and provocation tests that a dialysed extract of Western red cedar lost its potential to produce a bronchial reaction, thus excluding the possibility of small quantities of high molecular weight substances acting as antigens. On the contrary, by positive results in their provocation tests with plicatic acid, which is the major fraction (30 - 4- % of the extract) of the non-volatile components of Western red cedar [1], they showed that this constituent is probably the cause of the respiratory symptoms.



Plicatic acid

Plicatic acid produced bronchial reactions only in patients who also reacted to the Western red cedar extract. The authors suggested that this inhalation behaviour was an allergic reaction [4]. On the other hand investigations by Japanese authors [14,20], carried out between 1970 and 1972, showed positive findings to an aqueous extract of Western red cedar in the skin tests, inhalation test, Prausnitz-Küstner reaction and histmine release *in vitro*. Purification of this extract by gel-filtration on Sephadex yielded an active fraction having a molecular weight of about 100.000 and consisting mainly of polysaccharides. Further study of Western red cedar asthma would be worth wile.

Special troubles with the fine wood dust of Mansonia (*Mansonia altissima*) resulting in primary irritation of the mucosae, allergic rhinitis and bronchial asthma are reported from Italy, where this species is frequently used as a substitute for European walnut [3,6,7,22,25]. Gaffuri et al. (1968) [7] state that up to 26,7 % of the employees in woodworking factories in Padua suffer from respiratory disorders due to Mansonia wood dust.

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Table 8 Wood species known or suspected to cause allergic bronchial asthma and rhinitis

Botanical name	Family	Trade name (s)	References
Abies alba Miller	Pinaceae	Whitewood, Silver fir	24,31,39,41
Abies grandis Lindley	Pinaceae	Grand fir	24,60
Acacia melanoxylon R.Br.	Leg.- Mim.	Australian blackwood	10,44,46
Acer sp.	Aceraceae	Maple	46,50
Afzelia africana Sm	Leg.- Caesalp.	Afzelia, Lingué	14
Afzelia bipindensis Harms	Leg.- Caesalp.	Doussié	14
Aningeria robusta A.Chev.	Sapotaceae	Anegré, Osan	31
Aucoumea klaineana Pierre	Burseraceae	Okumé	9,26,31,47,58
Baikiea plurijuga Harms	Leg.- Caesalp.	Rhodesian teak	40,42
Baillonella toxisperma Pierre	Sapotaceae	Moabi	39
Buxus sempervirens L.	Buxaceae	Boxwood	18,36,60
Cedrus libani Barr.	Pinaceae	Cedar of Lebanon	21,26
Chamaecyparis lawsoniana Parl.	Cupressaceae	Port Orford cedar, Orgeon cypress	54,57
Chlorophora excelsa Bentham & Hooker	Moraceae	Iroko, Kambala	9,20,26,31,38,42
Dalbergia melanoxylon Guill. & Perr.	Leg.- Papilion.	Grenadill	39
Dalbergia nigra All.	Leg.- Papilion.	Brazilian rosewood, Jacaranda	24,26,39
Dalbergia retusa Hemsl.	Leg.- Papilion.	Cocobolo	16,22,63
Dipterocarpus alatus Roxb.	Dipterocarpaceae	Yang, Gurjun	62,63
Entandophragma angolense C.DC	Meliaceae	Tiama	63
Entandophragma utile Sprague	Meliaceae	Sipo, Utile	47
Fagus sylvatica L.	Fagaceae	Beech	24,26,31,35,39,41
Fraxinus excelsior L.	Oleaceae	Ash	26
Gonystylus bancanus (Mig.) Baillon	Thymelaeaceae	Ramin	28,39,41
Gossweilerodendron balsamiferum Harms	Leg.- Caesalp.	Agba, Tola branca	63
Juglans regia L.	Juglandaceae	Walnut	24,26,31,39

Table 8 (continued)

Khaya spp.	Meliaceae	African mahogany	1,25,26,31,47,56
Larix decidua Miller	Pinaceae	Larch	25,26,31,39
Lovoa trichilioides Harms	Meliaceae	African walnut, Dibetou	2,42,55
Magnolia obovata Thunberg	Magnoliaceae		61
Mansonia altissima A.Chev.	Sterculiaceae	Mansonia, Béte´	9,24,25,26,31,38, 39,41,51
Microberlinia brazzavillensis A.Chev.	Leg. - Caesalp.	African zebrawood	7
Millettia stuhlmannii de Wild.	Leg.- Papilion.	Panga-panga	26,42
Mitragyna stipulosa Kuntze	Rubiaceae	Abura	48
Oxystigma oxyphyllum J.Leonard	Leg.- Caesalp.	Tchitola	59
Pericopsis alata van Meuven	Leg.- Papilion.	Afrormosia	24,63
Picea abies Karsten	Pinaceae	Fir, Spruce	3,18,23,24,31,63
Picea mariana (Miller) B.S.P.	Pinaceae		11
Pinus palustris Miller	Pinaceae	Pitch pine	31
Pinus sylvestris L.	Pinaceae	Pine	31
Piptadeniastrum africanum (Hooker) Brenan	Leg.- Mim.	Dabema	33,38,48
Platanus acerifolia Willd.	Platanaceae	English plane	26
Populus tremula L.	Salicaceae	Poplar	26,31,39
Pouteria surinamensis Eyma	Sapotaceae	Abiruana	4
Pseudotsuga menziesii Franco	Pinaceae	Oregon pine, Douglas fir	31,39
Pterocarpus angolensis DC	Leg.- Papilion.	Muninga, Kejaat	2,41,42
Quercus robur L.	Fagaceae	European oak	26,31,39,41,53,56
Santalum album L.	Santalaceae	Sandal wood	18
Sequioa sempervirens Endl.	Taxodiaceae	Redwood, Sequioa	8,10,13,26,43
Shorea spp.	Dipterocarpaceae	Meranti, Lauan, Seraya	9,32

Table 8 (continued)

Swietenia macrophylla King	Meliaceae	American mahogany	26
Tarrietia utilis Spreng.	Sterculiaceae	Niangon	9,24,25,31,41,51
Tectona grandis L.	Verbenaceae	Teak	9,18,20,24,25,26, 31,41
Terminalia ivorensis A.Chev.	Combretaceae	Framiré	9,47
Terminalia superba Engler & Diels	Combretaceae	Limba	24,26,31,41
Thuja occidentalis Carr. (north America)	Cupressaceae	White cedar	15,50
Thuja plicata D.Don (north America)	Cupressaceae	Western red cedar	7,12,19,29,37,47
Thuja standishii Carr. (Japan)	Cupressaceae	Nezuko, Kurobe (Jap.)	30
Tieghemella africana Pierre	Sapotaceae	Douka, Ukola	1,14,58
Tieghemella heckelii Pierre ex Chev.	Sapotaceae	Makoré	5,9,24,25,26,27, 38,39,41,47,48, 52,62
Triplochiton scleroxylon K.Schum.	Sterculiaceae	Obeche, Abachi	6,24,25,26,31,34, 39,41,45,63
Turraeanthus africanus Pellegr.	Meliaceae	Avodiré	9,62
Zschokkea aculeata Ducke	Apocynaceae		17

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IV. Extrinsic allergic alveolitis

The formation of complexes between antigen and antibody can lead to the activation of the complement system followed by a series of hypersensitivity disorders. These are mostly severe respiratory difficulties occurring within 4 - 8 hours after exposure to organic dusts of different origin. The representative disease of this group is the so-called 'farmer's lung'. The major symptoms and signs are coughing, fever, general malaise and apparent changes of the lung tissue. In most cases the disease at first resembles influenza. Scratch and intradermal tests will give *false positive*, rarely false negative reactions; only inhalation tests are reliable. A remarkable sign are immune complexes formed *in vivo*, detectable as precipitins in the patient's serum. The double diffusion test on agar plates (Ouchterlony-test) (Figure 13) or an immune fluorescence method are the most convenient procedures for detection of the precipitating antibodies [9]. According to Gell & Coombs [4] this Arthus-type reactivity is classified as a *type-III-allergy*, also named *pulmonary hypersensitivity*, *hypersensitivity pneumonitis* and *extrinsic allergic alveolitis*.

Several observations point towards the fact that an immediate anaphylactic response (type-I) is mandatory for initiating the first stage of the Arthus-reaction. As the lung is capable of sustaining all *four* types of immune injury in response to inhaled antigens the symptoms of allergic alveolitis are generally viewed today not as a single disease entity but a series of events which are regarded as a 'disease spectrum' [8].

A combination of immediate and late reactions in connection with the detection of precipitins in the patient's serum should be recognised as evidence for the possibility that an extrinsic allergic alveolitis is present in a woodworker.

Only a few samples have been described of extrinsic allergic alveolitis caused by dusts of exotic and domestic species in woodworkers, as shown in Table 9.

Table 9 Wood species causing *extrinsic allergic alveolitis* (type-III-allergy) (characterised by precipitating antibodies)

Species	Trade name
Caesalpinia echinata Lamb.	Pernambuc
Chlorophora excelsa Bentham & Hooker	Iroko, Kambala
Diospyros sp.	Ebony
Gonystylus bancanus (Mig.) Baillon	Ramin
Khaya spp. and *Swietenia spp.*	Mahogany
Sequoia sempervirens Endl.	Redwood
Thuja plicata D.Don	Western red cedar

The first observation and investigation, by Cohen et al. (1967) [1], was a report on a 38 year old Redwood sawyer (*Sequoia sempervirens*). The patient's serum contained more antibodies against Redwood extracts than did the sera of the similarly exposed coworkers and he reacted to at least one antigen in Redwood sawdust against which

only the patient's serum reacted. The authors could not decide whether the patient's pulmonary injury resulted from reactions to the inhaled Redwood dust or the fungal particles covering the bark.

Sosman et al. [11] reported a case of a patternmaker with shortness of breath, coughing and wheezing after extensive exposure to mahogany (*Khaya spp.* or *Swietenia spp.*) The symptoms developed gradually over 4 - 6 hours after exposure only to Mahogany wood dust. Precipitating antibodies only against aqueous extracts of Mahogany extract could be demonstrated in the patient's serum. In a second case some hypersensitivity symptoms after exposure to Cedar dust occurred. The species was not identified. Skin tests were negative, but precipitating antibodies could be demonstrated in the serum. Sosman et al. wrote: 'the solubility of the wood dust antigens in aqueous or alcoholic solutions suggests that protein or carbohydrate moieties may be involved although the participation of haptens cannot be ruled out'.

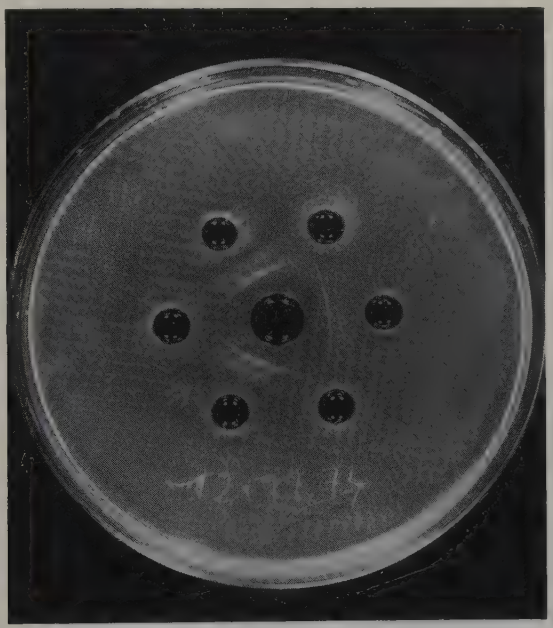

Figure 13 Precipitating antigen-antibody-complexes demonstrated by gel double diffusion technique (Ouchterlony-test). Middle hole: serum of the allergic patient; other holes: different concentrations of the antigenic extract

Gandevia et al. [3] observed delayed reactions in two woodworkers occurring between four to six hours, and also at night, due to the inhalation of dust of Western red cedar (*Thuja plicata*). Though they failed to show precipitin lines in the Ouchterlony-test using the patient's serum and Western red cedar extracts, the symptoms closely resem-

bled those of type-III-reactions. Similar reactions were also seen by Pickering et al. in 1972 [10]. The serum of one patient who was allergic to Iroko (*Chlorophora excelsa*) gave a positive precipitin reaction only to the Iroko extract. Though Girard et al. [6] gave no detailed information on their cases they could demonstrate in one patient precipitaing antibodies against domestic wood extracts by the Ouchterlony technique; the species were not identified.

An interesting case was reported by Howie et al. in 1976 [7]: a 34 year old man with a two-year history of episodes of breathlessness, coughing, shivering and tiredness which occurred 4 - 6 hours after periods of heavy exposure to Ramin wood dust (*Gonystylus bancanus*). The patient's history, the reduction of transfer factor, and the demonstration of precipitins to Ramin dust extracts in his serum supported the diagnosis of an extrinsic allergic alveolitis. Gheorghiu et al. [5] described the occurrence of precipitin lines found in the serum of two patients working with Ebony (*Diospyros sp.*) and Pernambuc (probably *Caesalpinia echinata*). No further details were given on the suspected wood species.

These short references to articles of the last twelve years show how important it is to distinguish between those cases of allergic alveolitis caused by the woods themselves [12] and the fungal material associated with woods or trees. *Most of the cases* of extrinsic allergic alveolitis described in the literature are due to spores of fungi growing on or in the trees as for example 'maple-bark disease' [2] and 'bagassosis' [13].

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V. Adenocarcinoma of the nasopharynx in woodworkers

Introduction

Inhalation of wood particles during machining, sanding, and other woodworking processes may develop - besides asthmatogenic symptoms - adenocarcinoma of the nasopharynx, especially when continued for many years. This observation was first made by Esme Hadfield and first published by Macbeth in 1965 [82]. It had been noticed in the area around High Wycombe (Buckinghamshire, England) that a significantly greater proportion of people whose occupation was chiefly associated with woodworking developed adenocarcinoma of the nasopharynx than in the rest of the population. Generally, malignant diseases of the nasopharynx are rare in the world population; for example in white populations nasopharyngeal cancer comprises only 0,25 % of all malignant tumors [16]. Only among southern Chinese and some Kenyan Highlanders in Africa have higher proportions of this cancer been observed [31,39,108].

Occurrence

Macbeth recognised during his studies that out of a total of twenty patients with adenocarcinoma of the nasopharynx no less than fifteen were woodworkers employed in the woodworking indutry of High Wycombe (England) in the manufacture of wooden chairs. This was statistically highly significant. Similar observations by Hadfield [59] and others corroborated these observations as a most striking feature of woodworker's diseases in southern England [1,5,6,60,61].

The adenocarcinoma of the nasopharynx is defined as a cancer of the nasal mucosa caused by a carcinogen which penetrates the mucus glands and initiates carcinogenesis.

The furniture industry in England is mainly centred in the town of High Wycombe and the surrounding villages. 12 % of all wooden furniture and 80 % of all chairs manufactured in England are produced there. More than 3000 men are employed as woodworkers in this area, most of them being carpenters, joiners, turners, cabinet makers and chair makers, wood sawyers and wood machinists [60,61]. In these workers three pathological changes of the nose have been distinguished:

- adenocarcinoma of the ethmoid air sinuses
- squamous metaplasia of the mucous membrane covering the anterior ends of the middle turbinates
- vasomotoric allergic rhinitis and nasal polypi.

A national survey revealed that adenocarcinoma of the nasopharynx was highly significant among woodworkers when compared with occupations in other indutries [5]. Similar observations and studies on malignant diseases of the nasopharynx in other European and overseas countries following the first publications of Acheson [1] and Hadfield [59] confirmed the English findings [14,28,29,96]. Table 10 gives a survey of the papers published between 1965 and 1980 in this field. It is obvious that in countries where furniture and woodworking industries are concentrated in a few regions such as England, Belgium, France, Denmark, Australia and the United States similar observations have been published. However the discovery of an increased risk of nasal cancer

Table 10 Survey on the excess of adenocarcinoma of the nasopharynx in woodworkers observed in different countries

Country	Author	Year	Adeno-carcinoma	Period	Refer.
England	Acheson	1967	13/17	1956 - 1965	1
England	Acheson	1968	37/45	1956 - 1967	2
England	Acheson	1972	34/107	1961 - 1966	5
France	Adenis	1973	10/18	- 1970	7
Denmark	Andersen	1976	12/17	1964 - 1974	9,10,11
Germany (West)	Andrée	1977	9/26	1959 - 1975	12
France	Bourguet	1974	27/45	1950 - 1973	24
USA	Brinton	1977	8/37	1965 - 1974	25,26
France	Curtes	1977	15/21	1964 - 1974	34
Belgium	Debois	1969	12/20	1958 - 1968	35
Netherland	Delemarre	1971	11/16	1956 - 1968	36
France	Desnos	1973	6/7	1964 - 1972	37
Sweden	Drettner	1979	0/715	not known	40
France	Egret	1972	10/18	- 1970	42
Sweden	Engzell	1978	19/36	1961 - 1970	43
Sweden	Engzell	1979	22/44	1960 - 1972	43
France	Fombeur	1972	3/5	-	45
France	Gignoux	1968/1973	17/53	1952 - 1972	52-54
France	Guinchard*	1972	30/32	1945 - 1971	7,8,90
England	Hadfield	1970	29/35	1955 - 1970	59-62
Australia	Ironside	1975	14/19	1965 - 1975	9
France	Leroux-Robert	1974	26/45	1957 - 1973	78
Germany (East)	Löbe	1978	13/18	1931 - 1977	80
Austria	Löffler	1972	2/4	1960 - 1970	81
England	Macbeth	1965	15/20	1951 - 1959	82
France	Marandas	1974	18/38	1957 - 1972	83
Denmark	Mosbeck	1971	4/7	1956 - 1966	88
England	Mould	1976	4/10	1960 - 1974	89
France	Peyresblanques	1978	177/567	not known	93
Finland	Tola	1980	2/51	1970 - 1973	111
France	Trotel	1976	13/36	1964 - 1974	112
France	Walter	1976	15/26	1962 - 1976	115

* Guinchard's publication contains the cases of Gignoux, Mounier-Kuhn and Gaillard [47,52,53,54,90]

is not restricted to the furniture industry alone but is also known to occur in the boot and shoe industry [4,6,62]. Workers are exposed to fine dust both in the furniture and in the boot and shoe industry, but in furniture makers the increase of cancer is limited virtually to *one* histological type of tumor: the adenocarcinoma, whereas in the boot and shoe industry *all* histological types of tumors are increased. In the latter case the fine dust derives from leather, fibre board, rubber, cork and plastic material, the only link between these two industrial tumors being the fact that fibre boards contain fibres of wood [4,6]. In a survey of 19 cases of adenocarcinoma of the nose and paranasal sinuses from Australia Ironside [69] could demonstrate that in seven cases the patients were involved in woodworking. Contrary to the experience in England where the *fine* dust in cabinet maker's and furniture maker's shops has been blamed for the occurrence of the malignant disease he pointed out that in Australia carpenters and sawmillers were exposed to *coarse* dust at work. The author himself gave three possible explanations for this discrepancy:

- saw milling may be a proportionally larger industry in Australia, furniture making the larger industry in England
- the timbers used in Australia may be drier than the woods used in England
- the varieties of the timbers used may be different; it seems possible that some varieties of wood contain carcinogens and others do not.

In contrast to the findings and observations in England, France, Belgium and the Netherlands neither Ball [18,19], an anonymous author [13] in Canada, nor Sanchez-Casis (Mayo Clinic) [98], or Brinton [25] in a survey of U.S. counties, nor Gülzow [57] in West-Germany, Löffler [81] in Austria and Tola [111] in Finland could find an excess of adenocarcinoma of the nasopharynx among woodworkers. In a second, more accurate case-control-study based on the data obtained from a special region of furniture industry in North Carolina Brinton [26] had to retract his first statement conceding that a four-fold risk of nasal cancer is linked to the occupation of furniture workers. Even Mould [89] could document an association between woodworking and excess of adenocarcinoma of the nasopharynx in areas where the woodworking (furniture) industry was concentrated. Similar observations were noted by Andrée in a recently published first investigation of woodworker's adenocarcinoma in West-Germany [12]. In England and France adenocarcinoma of the nasopharynx in woodworkers has become a prescribed disease under the National Insurance Regulations [60], but not in other European countries and the United States due to defiency of statistic material [12,21,57].

Development of adenocarcinoma of the nasopharynx

Adenocarcinoma is a slowly growing disease resulting from a long continued exposure to a minor irritant (Hadfield 1971) [60]. The basis of this definition is a long latent period and the high average of the workers involved [1,10,35,37,45,60]. Fig. 14 a - c shows the site of the ethmoid and nasal cavities. The observed latent periods range from 28 to 45 years (Hadfield 1971) [61]. Similar data are contributed by Acheson [2]: 27 to 69 years with an average of 43. French authors calculated an average of 40 years [7,52,78,115]. Most of the patients were in the 45 to 65 age group (Table 11).

Table 11 Types of wood species to which woodworkers with adenocarcinoma of the nasopharynx were exposed during their working life

Author	Year	Wood species	Years	Cou
Acheson	1976	Beech,Mahogany,Oak,Walnut,Sapele (few),others	43	GB
Adenis	1973	No information	39	F
Andersen	1977	Beech,Mahogany,Oak,Teak,Walnut	38	DK
Andrée	1977	Beech,Fir,Khaya,Limba,Makore,Oak,Oregon pine Pitch pine, Spruce	35	D
Ball	1968	Birch,Cedar,Cherry,Hemlock,Mahogany,Maple	no inf.	CDN
Bourguet	1974	No information	no inf.	F
Curtes	1977	Ash,Chestnut,Khaya,Oak	42	F
Debois	1969	Beech,Oak	no inf.	B
Delemarre	1971	Hard woods	no inf.	NL
Drettner	1979	No information	no inf.	S
Egret	1972	Beech,Khaya,Oak,Pine,Poplar	42	F
Engzell	1978	Birch,Mahogany,Oak,Teak	ca.25	S
Engzell	1979	Oak (one case)	45	S
Fombeur	1972	Cherry,Chestnut,Fir,Gaboon,Oak,Okumé, Poplar,Walnut	20	F
Gaillard	1975	Cherry,Lime,Oak,Walnut	no inf.	F
Gignoux	1968	Bété,Moabi	38	F
Guinchard	1972	Afrormosia,Beech,Brazilian rosewood,Chestnut, Dibetou,Khaya,Macassar,Makoré,Mansonia, Moabi,Niové,Oak,Okumé	34	F
Gülzow	1975	Beech,Oak	44	D
Hadfield	1971	Beech,Elm,Oak	38	GB
Ironside	1975	Australian native timbers (e.g. *Eucalyptus spp.*)	30/35	AUS
Leroux-Robert	1974	Cherry,Chestnut,Iroko,Niangon,Okumé,Pine, Poplar,Sipo,Walnut	40	F
Löbe	1978	Native woods of Middle Europe	40	GDR
Löffler	1972	No information	5	D
Marandas	1974	Bosse,Brazilian rosewood,Chestnut,Elm,Khaya, Makoré,Mansonia,Oak,Okumé,Sipo	38	F
Mosbeck	1971	Beech,Birch,Mahogany,Maple (few),Teak	38	DK
Peyresblanques	1978	No information	47	F
Robinson	1971	Maple; other coniferous species	no inf.	USA
Trotel	1976	Beech,Cherry,Chestnut,Iroko,Khaya,Oak, Pine,Poplar,Sipo	43	F
Walter	1976	Beech,Oak	20/30	F
Tola	1980	Oak	43	SF

Cou = country. Fourth column: average duration of exposure to wood dust

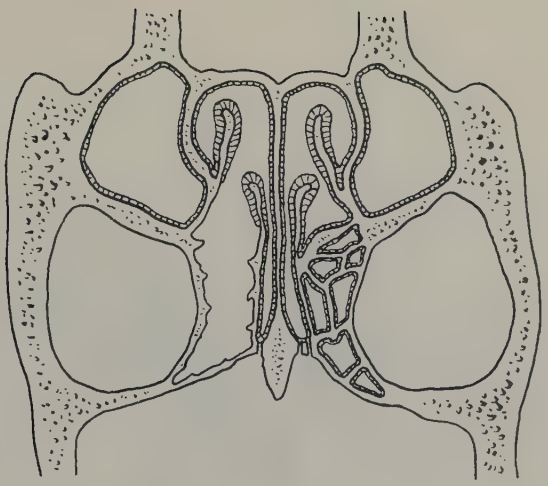


Figure 14 a Frontal cut through the rhinobase on the level of the ethmoid (on the left side the ethmoid cells are removed)

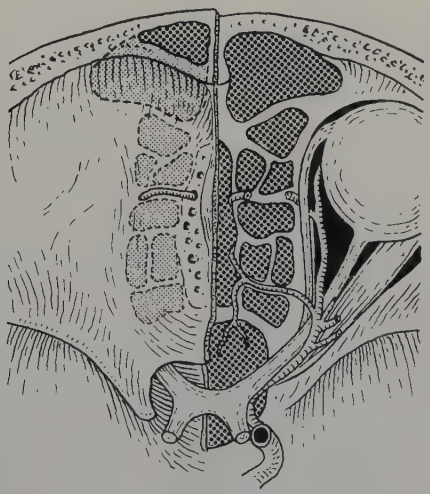


Figure 14 b Frontal base of the skull, intracraniel view, including ethmoidal arteries (left: cavities transparent; right: roof of ethmoid and orbita removed)

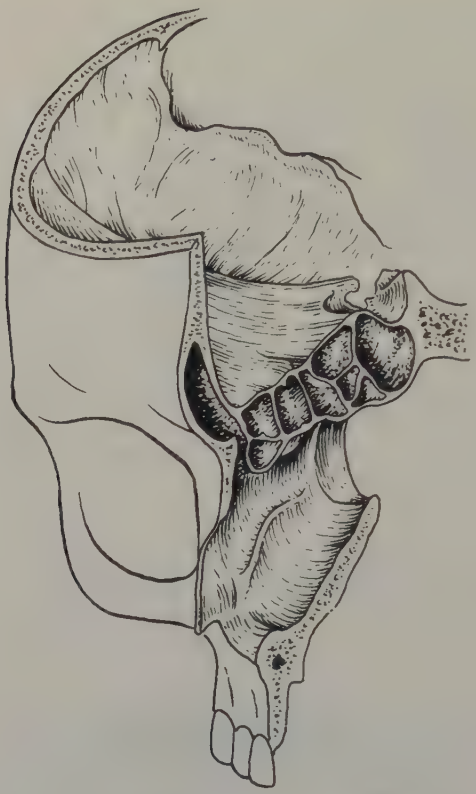


Figure 14 c View of the front of the base of the skull with nasal cavities

Before examining the development of adenocarcinoma a look at the factors which determine the direction of the upper respiratory pathways seems necessary. Inspiratory and exspiratory pathways are shown in Figure 15.

The air inspired during inhalation is first directed to the levels of the middle turbinate then downwards and backwards towards the posterior deoana. The greater part of the air impinges on the anterior end of the middle turbinate. After that it passes backwards between it and the septum. Very little, if any, reaches the orifices of the paranasal sinuses. The greater part of the expired air is filtered during the passage through the respiratory tract before it enters the sinus. This air only contains very few particles, so it seems improbable that the carcinogens enter the sinus by this route. The nasal mucosa of a healthy person is covered with a layer of mucus in which most of the particles entering with the inspired air are trapped. By the action of the cilia this con-

Figure 15 Air currents. Left: stream of inspired air. Right: direction of the exspired air streams, the eddy currents carry some of the exspired air in the direction of the sinus orifices (from [60])

taminated mucus is continually directed into the nasopharynx where it is eventually swallowed [60]. Inhalation of wood dust particles has to be imagined as follows: only a small part of the dust entering the nose is caught by the hairs in the nasal vestibules and only a small part passes into the lungs, most of the dust being deposited in two main areas, firstly on the anterior end of the nasal septum, just behind the mucocutaneous junction, secondly on the anterior end of the middle turbinate. A greater deposit of the dust is found on that side of the nose where the air way is better. Only in few people is the dust distributed equally on both sides [60].

Hanslian et al. [63] as well as Hounam et al. [66] have examined the size of dust particles and the levels of airborne dust in woodworking factories. Both groups concluded that 3/4 of the dust particles have a diameter of 5 μm. Scanning electron microscope examination showed that most of the particles are fibrous or flat in character. Furthermore their large surface area and area to volume ratio may facilitate the leaching of soluble toxic constituents.

It is therefore suggested that adenocarcinoma starts at the anterior end of the middle turbinate where most of the dust is deposited. The mucosa of the middle turbinate is richly supplied with mucous glands, whereas the antral mucosa is not. This mucosa undergoes squamous metaplasia during inhalation and permits the deposition of the fine dust. The squamous metaplasia of the mucous membrane covers at least 70 % of the

anterior ends of the middle turbinate. It seems that these changes are non-specific, i.e. they are not only produced by the inhalation of wood dust but may be caused by inhalation of any dust. The deposited dust is not carried away by ciliary action and possibly may get into the mucous glands in solid form or in solution. From this point the tumour then invades the ethmoid air cells [60]. Prolonged contact of the mucosa with the dust occurs because the wood dust depresses mucociliary clearance. In workers with impaired mucociliary clearance certain regions of the mucosa will be subjected to higher concentrations of certain soluble carcinogens than in people with normal clearance. A carcinogen in the dust penetrates the mucus glands and initiates carcinogenesis in the nasal mucosa itself.

In fact, Andersen [10,11] as well as Black [22] could prove that the mucostatic factor is of importance in the development of the adenocarcinoma. Both found that the mucus transport rates which are normally 5 mm/min are diminished to 1 mm/min or lower in woodworkers. Andersen's findings revealed that the number of mucostatic subjects is directly proportional to the wood dust concentration. Black's measurements of mucociliary clearance from the anterior end to the middle turbinate in woodworkers and in controls disclosed that there was only slow or almost complete stasis in woodworkers, which means that in woodworkers mucociliary function is significantly impaired.

In other words: particles inspired by inhalation will be entrapped in the mucus but will not be carried away if there are no cilia to propel it: if the wood dust contains a carcinogen its prolonged contact with the mucous membrane would provide it with an excellent port of entry to the anterior ethmoid air cells lying immediate behind; alternatively the tumour originates on the anterior end of the middle turbinate, just where the dust is deposited, and then grows by direct extension into the anterior ethmoidal air cells [60]

Theories on the etiological factors of woodworkers' adenocarcinoma

Shortly after the discovery of the great significance of adenocarcinoma in woodworkers some authors suggested the carcinogen being an agent that could be derived from the glues, stains, varnishes, polishes or other sources which the woodworkers inhale during their working time. However, a glance at the workshops where timbers are cut, sawn, joined and turned, cabinets and furniture are made, sanding machines are used and other woodworking processes are carried out, show that there is only one environmental factor common to all those involved: the exposure to wood dust. For example wood machinists, joiners and turners are not exposed to glues and polishes to any appreciable extent, whereas cabinet makers, chair makers and furniture makers use glue frequently, but the risk of developing adenocarcinoma of the nasopharynx in a turner is similar to that in a cabinet maker. Secondly, it has been suggested that cigarette smoking could play a role, but this cannot be regarded as a primary causal factor because smoking is such a common habit among the normal population that nasopharyngeal adenocarcinoma would not be such a rare tumour as it is.

As woodworkers are not allowed to smoke at work, snuff taking is a traditional habit especially among English woodworkers. Acheson [7] as well as Hadfield [58]noticed

that only a few of their adenocarcinoma patients were snuff takers and Andersen as well as Tola [9-11,111] found no history of snuff taking in their cases at all. Although snuff taking cannot be taken into account seriously it must be considered as a contributing factor for the etiology of this cancer. Considering these facts most of the authors of papers dealing with woodworkers' adenocarcinoma, including Macbeth in his first publication of 1965 [82], came to the conclusion that the primary causal factor must be some chemical constituent of the wood dust or the wood itself.

The period in which the woodworkers were exposed to the wood dust or particles was always long. Based on the observations from England and France the average time ranges from 38 to 43 years (see Table 11), which means that these patients have been exposed to large amounts of fine dust at a time when dust extraction by exhaust ventilation was substantially poorer than today. As better conditions and machinery in woodworking operations were introduced to the woodworking indutries only after World War II, it is obvious that the period of minimally efficient exhaust ventilation lay in the years between 1920 and 1940. One of the authors suggests that 'the hazard to health are now probably very different from what they were before the war' [13], whereas Hadfield [61] states that 'the maximal incidence of this malignant diseae is with us at the present and perhaps corresponds to the period of minimal exhaust ventilation of 1920 - 1940'. However, Desnos and co-workers point out [37] that three of their patients, aged 37 to 42 years, developed adenocarcinoma of the nasopharynx although they had benefitted from modern exhaust ventilation installed *after* the World War II. Kraus et al. [75] estimated recently that 50 - 100 new cases of nasal cancer develop every year in the woodworking industry in West-Germany. Pochin [94] estimated about 700 new cases per year in the United States.

During their working life most of the furniture-, cabinet- and chair-makers as well as wood machinists, joiners and turners were exposed to a wide variety of timbers. In most cases the men did not know the origin or the botanical classification of the species they worked with but usually they blamed the 'foreign woods' because of their aromatic and irritating properties [6,11]. In England, especially in the High Wycombe area, native timbers like Beech, Elm, and Oak are used [6,61], in other countries wood species are used which are different from the native timbers of England and France. Table 11 (p. 144) gives a survey of the wood species used by workers who developed adenocarcinoma of the nasopharynx in Europe, Australia and the United States. None of the wood species are common to all cases; therefore the character of the hypothetical carcinogenic constituent(s) of the wood or the wood dust seems to be connected not with a certain timber or a group of timbers (family?), but with *all* timbers used.

Moulds and fungi

Delving into the theories of the etiological factors of woodworkers' adenocarcinoma reveals some furhter interesting points. In 1968 Acheson [2] detected some relationship between nasal cancer in the boot and shoe industry and adenocarcinoma in the woodworking industry, the only difference being the fact that in furniture makers' cancer the increase was limited to the adenocarcinoma whereas in the boot and shoe industry *all* histological types of tumours were increased. He tried to explain this by

suggesting the possible occurrence of carcinogenic metabolites of moulds and fungi in the organic dust of the manufactured materials (wood, leather, etc.) Later (1976) [6] he discarded this hypothesis and postulated a new one declaring that the only link between these two industrial tumours is the fact that fibre boards contain wood fibres.

Tar

Machining operations such as sanding result in the development of high temperatures which may modify the constituents in the wood dust and particles so that they differ from and are possibly even more numerous than those of the wood substance itself [11,63]. Gülzow [57] in his paper on the first case of adenocarcinoma in a woodworker observed in West-Germany some years before [23], followed up this idea by heating fine wood dust of Oak and Beech experimentally. Chromatographic analyses of the products obtained compared with analyses of the tar produced from the same species, revealed that during mechanical crushing (sawing, sanding, machining) the wood particles become exceptionally hot and thus undergo chemical changes. The author could state that inhaled fine wood dust produced during machining and sanding consists of wood tar *and* many different wood constituents; both groups may possess low carcinogenic properties. Permanent exposure to low concentrations of these compounds over a long period resulting in mechanical irritation caused by the fine dust particles themselves and chemical irritation caused by the constituents may be a possible source of the adenocarcinoma observed in woodworkers.

Tannins and tannic acids

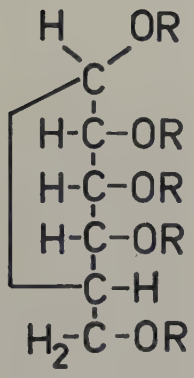
Tannins are a mixture of naturally occurring compounds which are able to transform skin into leather, (tanning), which is resistant to hydrolytic enzymes. This capability is based on the fact that the tannins are able, in low concentrations, to precipitate proteins. Due to their relatively low molecular weight of 500 to 3000 the tannins may diffuse through the intact skin. During the process of tanning they change the soluble and elastic proteins of the skin to insoluble and more rigid structures. Chemically tanning is thought to depend on the cross-linking of free amino groups of the protein polypeptide chains. The phenolic hydroxy groups of the tannins acting in this process by forming a network of intermolecular bonds [46,99,100,107]. According to Freudenberg [46] tannins may be classified quite generally into two groups:

- *hydrolysable tannins*, which on heating with mineral acids yield glucose or other sugars, and gallic acid and/or related polyphenolic acids
- *condensed tannins*, which form intractable precipitates on heating with mineral acids.

Examples of the two types are given on page 151. *General properties* of the tannins are that they absorb oxygen strongly, have reducing properties in alkali milieu and have a tendency to polymerisation and autoxidation resulting in amorphous substances of dark colour. Tannins are easily extractable from natural sources with water. They are said to play a role in cell metabolism.

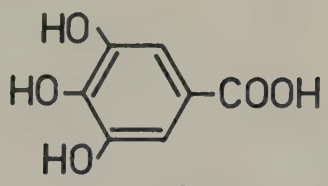
Condensed tannins are strongly suspected to possess carcinogenic properties [15,17, 67,68,74,87,95], especially some derived from catechins and leucoanthocyanidins

Hydrolysable tannins

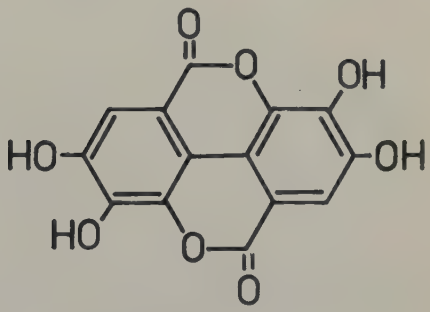


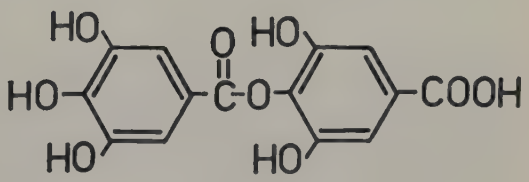
R = Gallic, Ellagic or Digallic acid

Gallic acid



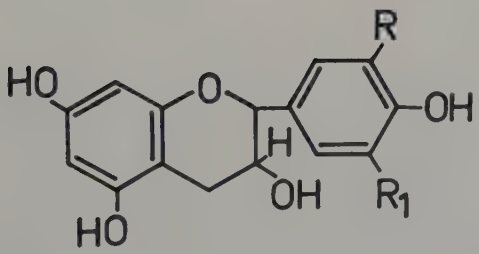
Ellagic acid





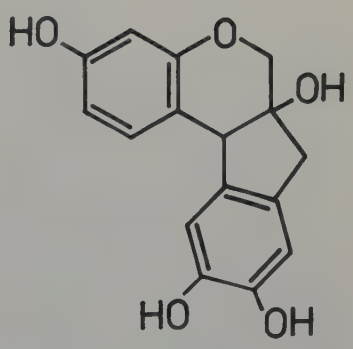
Digallic acid

Condensed tannins



Basic types of condensed tannins

Afzelechin	$R = R_1 = H$
Catechol	$R = OH, R_1 = H$
Gallocatechol	$R = R_1 = OH$



Brazilin

[17,41,46,64]. Investigations with extracts of plants and woods as well as with 'tannic acids' have shown that subcutaneous injection of the extracts produced tumours in mice and rats [48,49,50,72,114]. Condensed tannins evoked sarcomata at the site of injection as well as liver tumours, but only liver tumours were produced by extracts of hydrolysable tannins [72]. Extracts were prepared from different species including Quebracho (*Schinopsis lorentzii*), Acacia (*Acacia molissima*) and Eucalyptus (*Eucalyptus redunca*) all of which were of the condensed type, while Chestnut (*Castanea sativa*) and *Terminalia chebula* yielded hydrolysable tannins. Gallic acid and catechol itself did produce no carcinogenic activity. In 1971 O'Gara [49] started his experiments by studying extracts of different plants and woods for their sarcomogenic properties. Besides some adenocarcinomata of the duodenum and ovary he found that *Krameria ixina* induced subcutaneous sarcomas at the site of injection in 100 % of the rats [48], which he believed to be due solely to its content of tannin. In 1974 he followed up his studies by demonstrating that sarcomas *did not develop* at the site of injection of a fraction in the aqueous extract *after removal of tannins* by precipitation with caffeine [50]. In his experiments with fourteen plant and wood species *Acacia villosa* was the most intensely tumor-inducing one; *Acacia villosa* and *Krameria ixina* could be shown to be very rich in tannins.

Occurrence of tannins

More exact data on the occurrence of tannins are not available, but it seems that generally hard woods contain more tannin than soft woods with few exceptions (e.g. Poplar). Some important species are listed in Table 12.

Table 12 Occurrence of tannins in different wood species [20,38,58,72,84]

Timber	Species	Tannin (%) Wood	Bark
Beech	*Fagus sylvatica* L.	0,3 - 4	3 - 4
Black wattle	*Acacia molissima* Auct.non Willd.	-	- 25
Chestnut	*Castanea sativa* Miller	7 - 16	8 - 14
Cottonwood	*Populus deltoides* Marsh.	- 2	- 5
Golden wattle	*Acacia pycnantha* Bentham	-	- 35
Oak	*Quercus spp.*	3 - 13	4 - 16
Quebracho	*Schinopsis lorentzii* Engler	13 - 26	6 - 8
Redwood	*Sequioa sempervirens* Endl.	- 12	- 1
Spruce	*Picea abies* Karsten	0,1	5 - 18
Western hemlock	*Tsuga canandensis* Carr.	- 1	- 11
Western larch	*Larix occidentalis* Nuttal	- 7	- 11
Western red cedar	*Thuja plicata* D.Don	1,2 - 23,3	4,3
Western yellow pine	*Pinus ponderosa* Ect.	- 9	- 11

According to Guinchard [58] the following wood species are also rich in tannins, but the author does not mention the source of his informations: Acajou (*Swietenia spc., Khaya species*), Ako (*Antiaris africana* Engler), Buba (*Fagraea gracilepes* A.Gray) Difou (*Morus mesozygia* Stapf), Eucalyptus (*Eucalyptus spc.*), Iroko (*Chlorophora excelsa* Bentham & Hooker), Kikula (?), Moabi (*Baillonella toxisperma* Pierre), Mbandi (*Julbernardia brieyi* (de Wild.) Troup.?), Niove (*Staudtia stipitata* Warburg), Wacapou (*Vouacapoua americana* Aublet), Bété (*Mansonia altissima* A.Chev.), Mricoudi (*Weinmannia spc.*), Mtankoumi (*Gaertnera* cf *paniculata* Bentham) and Mrimehou (*Eugenia spc.*). Guinchard was the first to develop ideas in his thesis about the compounds responsible for woodworkers' adenocarcinoma. He and his colleagues [83,110] believe that the most likely explanation is that due to the ability of the tannins to precipitate proteins and to influence the cell metabolism, together with their carcinogenic properties, the tannins in the inhaled wood dust particles seem to be the substances which are most probably responsible for adenocarcinoma of the nasopharynx. This hypothesis may also be a possible explanation for the simultaneous occurrence of nasopharyngeal cancer in the furniture and the boot and shoe industry, as tannins are the only principal constituents which woods and leather have in common [3,60]. Thus Schoental broaches the question: 'it would be of interest to know whether the incidence of tumours is also increased among tanners, and whether it has some relation to the various tanning processes' [107]. Until now this question has not been answered.

α,ß-Unsaturated aldehydes and oxidation products

In 1973 Schoental [106] observed that 'spontaneous tumours' occurred in laboratory animals when fresh bedding of Red cedar or Pine was used. Already in 1966 Ferguson [44] had found that Red cedar chips in animal houses decreased the sleeping time of the animals to approximately 50 %. He supposed that some 'volatile material' in the Red cedar chips was responsible for these changes. In a report from Australia Sabine et al. [97] contributed the results of a study which showed that Red cedar bedding can restore the high incidence (100 %) of at least the mammary tumours in mice, when kept in cages in Australia but provided with Cedar shavings from the United States. Finally Vesell reported [113] the induction of three microsomal drug-metabolising enzymes in the liver of mice and rats kept on softwood bedding of Red cedar, Ponderosa pine or White pine. This induction was reversed when the chips were replaced by hardwood beddings of Beech, Birch or Maple. These four different observations indicate that certain wood species must contain some substance(s) which may be carcinogenic or have some other influence on the biological functions of laboratory animals; but more important is the fact that these observations may be seen in relation to the occurrence of malignant diseases of the nasopharynx in woodworkers.

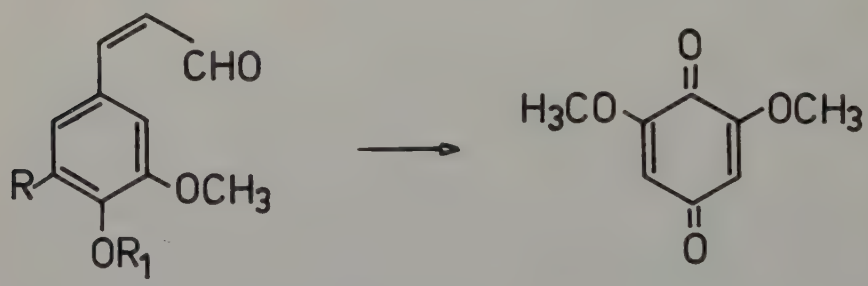
For a long time it has been known that simple compounds related to lignin (lignin precursors, degradation products) can be extracted from the wood itself or the wood smoke by organic solvents; these are coniferyl aldehyde and sinapic aldehyde. In the smoke of conifers coniferyl aldehyde predominates, while sinapic aldehyde is present mainly in that of angiosperm species [46,51,91,102]. Based on their experimental results in animals Schoental et al. suspected that such α,ß-unsaturated aldehydes, or their

oxidation products, or certain other derivatives possess carcinogenic properties [103 - 105]. For example they could show that the synthetic 3,4,5-trimethoxy-cinnamaldehyde, which is closely related to both wood aldehydes mentioned, was capable of producing squamous carcinomata in two rats, one of which was situated *in the ethmoid region*. In view of the rarity of nasal tumours in rats, these results seem very important in connection with the high incidence of nasopharyngeal tumours in woodworkers. Although the 3,4,5-trimethoxy-cinnamaldehyde is a synthetic product which does not occur in nature, the authors are convinced that it is not unlikely that the tumours induced by this and other aldehydes may be due to some of their metabolic products, which might include the sinapic aldehyde and/or the oxidation product 2,6-dimethoxy-1,4-benzoquinone [103-106].

In this connection it is remarkable that this simple quinone - 2,6-dimethoxy-1,4-benzoquinone has been isolated from more than 50 different plants and woods and is detected continously during investigations in our laboratory [65] (see also Systematic review, pp. 34 - 126).

One of the reasons for the frequent occurrence of 2,6-dimethoxy-1,4-benzoquinone in wood species may be associated with the wide distribution of phenoloxidases in the plant kingdom, and the fact that they are also produced by most wood-rotting fungi. Recent experiments with model compounds closely related to lignin have demonstrated that these enzymes are responsible for the oxidative degradation of wood lignin. The alkyl-phenyl bond in syringyl compounds such as syringylglycol-ß-guaiacyl ether and α-guaiacoxyacetosyringone is cleaved by the enzymes with formation of guaiacoxyacetaldehyde and guaiacoxyacetic acid, respectively, as shown on page 155.

Oxidation of syringylglycol-ß-guaiacyl ether (**1**) is initiated by pairing of phenoxyl and *p*-methylene-quinonoid radicals; participation of an electron pair of a methoxyl oxygen atom on the cyclohexadione ring leads to elimination of a molecule of syringylglycol-ß-guaiacyl ether. After subsequent stabilization of the resulting molecule by loss of a proton from the benzyl position (right column, p. 155) and rearomatization

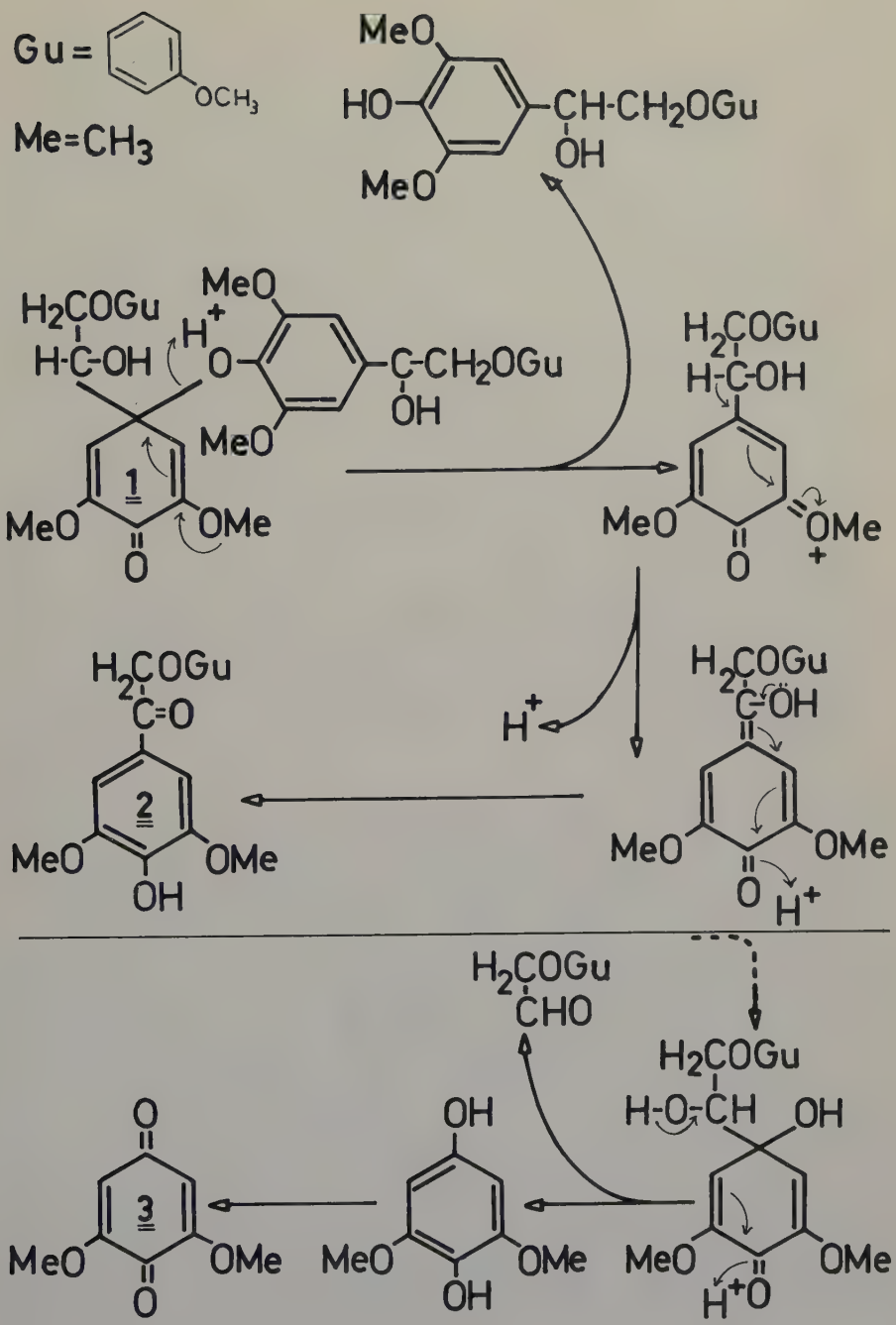


Coniferyl aldehyde $R = R_1 = H$

Sinapic aldehyde $R = OCH_3, R_1 = H$

3,4,5-Trimethoxy-cinnamaldehyde $R = OCH_3, R_1 = CH_3$

2,6-dimethoxy-1,4-benzoquinone

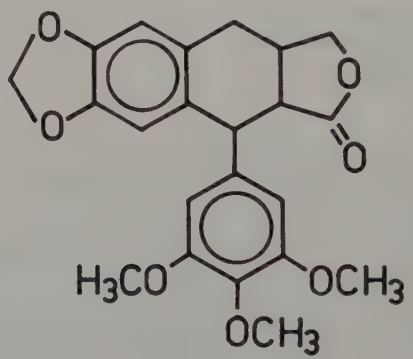

Gu =
OCH3
Me=CH3
MeO
HO
CH-CH2OGu
OH
MeO
H2COGu
H-C-OH
H+
O
C-CH2OGu
OH
MeO
1
MeO
OMe
O
H2COGu
H-C-OH
MeO
OMe
+
O
H+
H2COGu
C=O
2
MeO
OMe
OH
H2COGu
C-OH
MeO
OMe
O
H+
H2COGu
CHO
H2COGu
H-O-CH
OH
O
3
MeO
OMe
O
OH
MeO
OMe
OH
MeO
OMe
H+O

α-guaiacoxyacetosyringone (2) is obtained. Formation of 2,6-dimethoxy-1,4-benzoquinone (3) is achieved by oxidative cleavage of syringylglycol-ß-guaiacyl ether as shown in the row below (p. 155) [27,70,73].

Similar studies performed with vanillic acid, another intermediate product of fungal degradation of lignin, demonstrated that vanillic acid is oxidatively decarboxylated to methoxy-1,4-benzoquinone [76]. It may be imagined that these simple benzoquinones produced by phenoloxidases are also produced by the oxidative conditions connected with high temperatures during machining, sanding and other woodworking processes thus being involved in the induction of adenocarcinoma of the woodworkers. As already mentioned Schoental [106] succeeded in inducing squamous sarcomas at the site of subcutaneous injections in rats with 2,6-dimethoxy-1,4-benzoquinone.

Recent Ames-tests [8] with ether- and methanol-extracts of fine wood dusts of Obeche Beech, Limba, Mahogany, Oak and Walnut showed mutagenic acitivity of all tested extracts, especially with Obeche after addition of oxygenase. Fractions obtained by separation on Sephadex LH-20 columns revealed mutagenic activities mainly in the acetone water and cyclohexane-soluble parts of the extracts (K.Norpoth, private communication, 1980). Although no definite conclusions are deducible from these preliminary results the experimental data clearly indicate the direction which future investigations should take.

In this connection another investigation result seems worth mentioning. In the course of search for tumor inhibitors Kupchan et al. (1967) [77] discovered that an alcoholic extract of *Calocedrus decurrens* (Incense cedar) showed a significant inhibitory activity against cells derived from human carcinoma of the nasopharynx in tissue cultures. A systematic study led to the isolation of deoxypodophyllotoxin, which revealed to be the major cytotoxic principle of the Cedar extract.



Deoxypodophyllotoxin

A first indication of the association between nasal cancer and wood or wood products was given by Digby in 1941 [39]. In his opinion the increase of nasopharyngeal tumours observed in poor Chinese people might be due to their way of life: most of them live in native houses which are not ventilated and the fireplace is fed with poor quality wood. He suggested that the soot-laden atmosphere might irritate the nasopharyngeal lymphoid tissue and therefore predispose these people to contract malignant diseases of the nasopharynx. Clifford [30,31] discovered likewise a higher incidence of adenocarcinoma of the nasopharynx in Kenyan people who live in the colder areas of their country. He noted that this disease did not occur in the Highlands of Kenya, particularly the coast and northern province, which is dry and warm, and where cooking is generally undertaken outside the hut. In those regions of Kenya where the cancer occurs, exotic trees like Eucalyptus and Acacia species are used to provide firewood, mainly Wattle (*Acacia mearnsii* de Wild.), but also *Eucalyptus saligna* Sm, *Eucalyptus citriodora* Hooker as well as various indigenous *Acacia* species. Clifford's hypothesis is that inhalation of cooking fire smoke for several hours a day over a long period of years has some bearing on the distribution and incidence of this malignant kind of disease in Kenya.

Gibbard et al. [51] have, as already mentioned above, investigated the smoke of Chinese incense and of antimosquito coils for carcinogenic constituents by thin-layer chromatography. The above quoted sinapic aldehyde, coniferyl aldehyde, and other aldehydes were detected in the smoke and extracts of powdered Sandalwood (*Santalum album*), as a main component of Chinese incense, as well as in Coconut shell powder, and as the major constituent of antimosquito coils. Further studies of other important hard woods yielded the largest amounts of sinapic aldehyde in *Eucalyptus spc.* (3000 μg/g) and somewhat lower amounts in Beech (*Fagus sylvatica*) (800 μg/g) and Oak (*Quercus robur*) (500 μg/g).

This high concentration of sinapic aldehyde in *Eucalyptus* species, which might be assumed to occur also in Kenyan *Eucalyptus* species used as firewood, strongly support Clifford's hypothesis on the etiological factors of adenocarcinoma in the Kenyan population. The lower but nevertheless considerable yields of sinapic aldehyde in Beech and Oak throw further light on Schoental's ideas of the causal factors and associations between adenocarcinoma of the nasopharynx and the woodworking population in Europe, especially in those countries where Beech and Oak are frequently used (France, England, Belgium).

VI. Hodgkin's disease in woodworkers

At the same time when Acheson, Hadfield and Macbeth [1-6,59-62,82] recognised an excessive incidence of adenocarcinoma of the nasopharynx among woodworkers in England other authors noted a relation between the occurrence of Hodgkin's disease and the woodworking occupation [2,85]. In contrast to the localised adenocarcinoma of the nasopharynx Morbus Hodgkin is a disease of unknown etiology, characterised by enlargement of the lymph glands, hyperplasia of the lymphoid tissue in the spleen, liver and other organs, and anaemia.
The incidence of this disease seems to be slightly higher, but not as significant as woodworkers' adenocarcinoma. Cases have been observed in the Oxford area in England in wood and paper workers [2]. Milham from the United States found in 1967 an excess of woodworkers among men who died of Hodgkin's disease [85]; they included carpenters, cabinet makers, lumberjacks, lumber dealers, sawmill operators, sanders, crate makers, furniture factory workers, boat builders and papermill workers, especially beatermen. In a more detailed occupational mortality analysis nine years later [86] he reported particularly - besides other increases of different types of cancer in woodworkers - excessive incidence of Hodgkin's disease among paperworkers in the USA. Petersen's study of the Washington State and New York State death records revealed that carpenters and papermakers had the highest proportional mortality ratio [92]. Similar results were obtained by Greene et al. in 1978 [55]. Gufferman et al. compared in 1976 [56] different occupational groups, for example engineers, teachers, lawyers, nurses and physicians with woodworkers and found that woodworkers had a small increased risk of Hodgkin's disease.

The theories on the etiological factors are different. Some authors postulated the hypothesis that the increased risk of Hodgkin's disease in woodworkers is related to their occupational exposure to Pine pollen, but this theory was discarded quickly [32, 33,67,79,101,109]. Milham [85,86] as well as Acheson [2] believe that the causative factors are physical or chemical breakdown products of the wood which may be carcinogenic. Recent mature considerations indicate that an immunological mechanism may be the basis of Morbus Hodgkin.
Although this problem remains to be resolved by further investigations of mortality ratios as well as chemical studies and animal experiments, Greene tried to find a link between Hodgkin's disease and nasopharyngeal cancer in woodworkers when he blamed pentachlorphenol as a causal factor writing: 'pentachlorphenol is applied to lumber at many stages in its processing, beginning at the sawmill. Unrecognised exposure may occur among many wood utilising occupational groups. Thus it may be that the association between wood exposure and Hodgkin's disease and *perhaps nasal cancer* is related to the use of particular chamical preservatives' [55].

Final comment

All these investigations, national surveys on mortality ratios, chemical and animal experimental studies, theories on the causative factors, and other statements in the last two chapters still leave some discrepancies, unanswered questions and an unpleasant feeling.

- Why, for example, have only a few or no cases of adenocarcinoma of the nasopharynx been reported from West-Germany, Sweden and Finland, although it is known that a successful woodworking indutry exists in these countries?
- Did not the publications from England, France, Belgium, Denmark and the Netherlands draw attention to the possible simultaneous occurrence of this type of cancer in Germany and other Scandinavian States?
  Or may the lack of statistic material be due to the fact that the furniture industry is not concentrated in a particular region in these countries like in the High Wycombe area in England? This is not true for West-Germany, where a centre for the furniture, plywood and chipboard industry is settled in Westfalia (northwestern part of W-Germany).
- Is there stricter supervision of exhaust ventilation by factory inspectors and trade unions in West-Germany, Sweden and Finland which results in lower levels of airborne wood dust in these factories compared to other countries?

On the other hand it should be asked if *fine* wood dust is a problem at all, because Ironside [69] seems to be sure that nasopharyngeal cancer also occurs when *coarse* rather than fine dust is mainly present in the air of workshops etc., as he could demonstrate in Australia.

Finally it remains to be resolved if the maximum incidence of this malignant disease *is with us at the present* while it corresponds - due to the long latent period - to the time of minimal exhaust ventilation of the years 1930 - 1940 as Hadfield pointed out [61] or are the hazards to health today truly different from what they were before the the Second World War [13]?

The author believes that it is of the greatest importance to make every effort to find the causative factors of nasopharyngeal cancer on the supposition that they are truly substances from the wood. Fourteen years are gone since the discovery of adenocarcinoma of the nasopharynx in woodworkers; now it is time to stop discussions and start fundamental research, - as has been just been initiated in the four Nordic States of Denmark, Finland, Norway and Sweden [40,43] (B.Drettner, private commun. 1981) - with the aim of helping people employed in the woodworking industries so that they will not suffer in the next two decades from cancer that is being induced in their bodies *at the moment.*

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In Table 13 finally all those wood species are listed which are of less commercial value - sometimes only of local importance - but which have been blamed in the literature as being toxic, irritant, asthmatogenic, sensitising and otherwise injurious to health. In most publications the descriptions of the symptoms lack details. Exceptions are Campherwood (*Cinnamomum camphora*), 'Miva mahogany' (*Dysoxylon muelleri*), Aroeira (*Lithraea caustica*), Japanese lacquer tree (*Rhus vernicifera*) and White cedar (*Thuja occidentalis*)

Explanations: Leg.- Caes. = Leguminosae-Caesalpiniaceae
Leg.- Mim. = Leguminosae-Mimosaceae
Leg.- Pap. = Leguminosae-Papilionaceae

Table 13 List of timbers with less commercial value which have been mentioned in the literature as toxic, irritant and sensitising

Botanical name	Family	Trade name	Use	Symptoms	References
Acacia harpophylla F.Mueller	Leg.-Mim.	Brigalow	furniture, joinery	'Brigalow itch'	41
Acer spc.	Aceraceae	Maple	turnery,flutes,recorders	dermatitis	39,69
Albizzia ferruginea Bentham	Leg.-Mim.	Iatandza, Okuro	joinery, carpentry	irritation - nose	17
Albizzia lebbeck (L.) Bentham	Leg.-Mim.	Kokko, Siris	veneer,furniture, boat-build.,int.work	irritation - nose general malaise	7,20,32,35 65
Alstonia congensis Engler	Apocynaceae	Emien, Alstonia	plywood blind layers	irritation	70
Amoora polystachya Hook.f. & Jack.	Meliaceae	Tasua, Amora	construct.floor.,veneer	irritations	70
Andira inermis (Wright) H.B.K.	Leg.-Pap.	Rode kabbes, Angelin, Partridge	veneer,stairs,flooring construction	poisonous,narcotic, skin irritant	3,14,35
Araucaria angustifolia O.Kuntze	Araucariaceae	Paraná pine	constr.,join.,flooring, stairs,organ parts	fever,weakness muscle pains	10,25,70
Autranella congolensis A.Chev.	Sapotaceae	Mukulungu, Elang	flooring, construction	mucosal irritation	4
Baikiaea plurijuga Harms	Leg.-Caes.	Umgusi, 'Rhodesian teak'	veneer,railroad sleepers flooring	asthma, headache	43,44,45
Baillonella toxisperma Pierre	Sapotaceae	Moabi, Djave	boat-building,construc.	mucosal irritation	24,26
Balfourodendron riedelianum Engler	Rutaceae	Guatambu, Pau marfim	furniture, panelling turnery	poisoning	19
Baphia nitida Afz.	Leg.-Pap.	Camwood , Okoué	joinery	general symptoms	22,29
Cameraria belizensis Standley	Apocynaceae	White poison wood	local commerc.timber	poisoning	7,59
Cinnamomum camphora (L.) Presl.	Lauraceae	Campherwood	cabinets, chests	headache, giddiness	23,63,64
Copaifera bracteata Bentham	Leg.- Ceas.	Copaiba	furniture,turnery,const.	nausea, no appetite	23
Coumarouna odorata Aublet	Leg.- Pap.	Tonka, Tonguin	furniture, turnery	toxic effects	46,50,54,66, 67
Croton megalocarpus Hutch.	Euphorbiac.	Musine	floor.,railroad sleepers	irritation of nose, throat	25
Dipterocarpus alatus Roxb.	Dipterocarpaceae	Keruing, Gurjun, Yang	flooring, boat-building exterior joinery	skin irritations	46,50,54,66 67,70

Dysoxylon muelleri Bentham	Meliaceae	Red bean, Turnip wood, 'Miva mahog.'	furniture, cabinet work (Australia)	highly toxic	9,25,30,40 60,69
Erythrophleum guianense G.Don	Leg.-Caes.	Missanda, Tali Sasswood	flooring, construction frames, railr.sleepers	irritation - nose, throat, skin	15,33,35,48 65,70
Erythrophleum ivorense A.Chev.	Leg.-Caes.	Missanda, Tali Redwater tree	flooring, construction railroad sleepers	irritation - nose, throat, skin	33,35,48,65 70
Haematoxylon campechianum L.	Leg.-Ceas.	Logwood, Campeche	mainly for haematoxylin extraction	dermatitis	23,57
Juniperus procera Hochst.	Cupressaceae	African pencil tree	furniture, pencils	dermatitis	49
Juniperus virginiana L.	Cupressaceae	Virgin.pencil tree	furniture, pencils	dermatitis	5,8,42
Lithraea brasiliensis Marchal	Anacardiac.	Aroeira, Pao bugre	cabinet work	severe cont.dermatitis	6,31
Lithraea caustica (Mol.) Miers	Anacardiac.	Aroeira, Litre	cabinet work	severe cont.dermatitis	6,31
Lophira alata Banks ex Gaertner	Ochnaceae	Azobé, Ekki, Bongossi	water constructions railroad sleepers	itching, dermatitis	25
Lovoa trichilioides Harms	Meliaceae	Dibetou, 'African walnut'	furniture, veneer, cabinets, join., panelling	dermatitis, mucosal irritation	1,62,70
Manilkara huberi Standley	Sapotaceae	Massaranduba	turnery,constr.,handles	conjunctivitis	18,21
Melanoxylon brauna Schott	Leg.-Caes.	Braúna	water constr.,boat-buil.	dermat.,weakness	18
Microberlinia brazzavillensis A.Chev.	Leg.-Caes.	Zebrano, Zingana	furniture	irritant	71
Nesorgordonia papaverifera R.Capur.	Tiliaceae	Danta, Kotibé	constr.,floor.,joinery	irritation	70
Ocotea rubra Mez	Lauraceae	Louro vermelho	constr.,floor.,veneer	dermatitis	70
Oxystigma oxyphyllum J.Leonard	Leg.-Caes.	Tchitola	floor.,constr.boat-buil.	asthma, fever	61,62
Piptadeniastrum africanum Brenan	Leg.-Mim.	Dahoma, Dabema	constr.,railroad sleepers	sev.irrit.nose,throat	17,33,38,46
Pithecolobium arboreum Urban	Leg.-Mim.	Bahama Sabicu	furniture, joinery	itching,mucos. irritation	18,56
Prunus avium L.	Rosaceae	Cherry	furniture, join.,musical instruments	skin irritation	12
Pterygota macrocarpa K.Schum.	Sterculiaceae	Koto, 'African pterygota'	furniture, veneer,const.	stomach disturbances	47,70
Pycnanthus angolensis Warburg	Myristicaceae	Ilomba	plywood, construction	nausea, vomiting	25

Table 13 (continued)

Botanical name	Family	Trade name(s)	Use	Symptoms	References
Rhus vernicifera DC	Anacard-iaceae	Japanese lacquer tree	shoes, cabinet work lacquer production	allergic contact dermatitis, conjunctivitis	28,70
Robinia pseudoacacia L.	Leg.-Pap.	Robinia, False Acacia	turnery, flooring, construction	dermatitis, wood cutter's eczema	16,55,67
Schinopsis lorentzii Engler	Anacard-iaceae	Quebracho, Quebracho colorado	construct., railroad sleepers, tannin extraction	contact dermatitis	36,37
Staudtia stipitata Warburg	Myristicaceae	Niové	furniture, flooring	dermatitis	1
Tarrietia utilis Sprague	Sterculiaceae	Niangón	flooring, construction	dermatitis	52
Terminalia alata Roth et spp.	Combretac.	Indian laurel	construction, veneer	dermatitis	70
Terminalia ivorensis A.Chev.	Combretac.	Idigbo, Framiré	construct.,floor.,veneer	poisonous, asthma	13,70,71
Thuja occidentalis L.	Cupressaceae	White cedar	constr.,railroad sleepers boat-building	dermatitis, poisonous	8,27,53
Vateirea guianensis Aublet	Leg.-Pap.	Gele kabbes, Amargo	interior construction	dermatitis, conjunctivitis	58
Vateireopsis araroba (Aguiar) Ducke	Leg.-Pap.	Araroba, Goa powder tree	local construction wood	conjunctivitis, skin irritation	8,39
Xylia xylocarpa Taub.	Leg.-Mim.	Pyinkado	boat-biulding, tools construction wood	general health injuries, sneesing	11,20,34 70
Zollernia paraensis Huber	Leg.-Mim.	Pau santo, Tango, Coração de negro	furniture, joinery, construction	dermatitis, general symptoms	18

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Index of local, standard and trade names

	Standard name
Abang	Kambala
Abele	Poplar
Abenbegne	Tiama
Aborbora	Kotibé
Aboudikro(u)	Sapele
Acajou	(American) mahogany
Acajou d'Afrique	African mahogany
Acajou Sipo	Sipo
Acra	African mahogany
Adza	Moabi
Afara	Limba
African walnut	Dibetou
Afzelia	Doussié
Agamokwe	Makoré
Agbe	Avodiré
Agboin	Dabema
Aguano	American mahogany
Ahia	Kotibé
Ahmin	Ramin
Ake	Dabema
Akede, Ako	Antiaris (Bonkonko)
Akom	Limba
Akug	Sipo
Akuraten	Bossé
Alcornoque	Sucupira
Aliga, Aligna	Doussié
Allen ale	Zebrano
Almon	Light red meranti
Alona wood	Dibetou
Aluk	Cedrela
Amargoso	Peroba rosa
Amata prieta	Ipé
Amazokué	Bubinga
Ambila	Muninga
Ampira	Framiré
Andoum	Antiaris (Bonkonko)
Angouma	Okoumé
Anon	Wengé
Anyaran	Movingui
Apa	Afzelia (Doussié)
Apaya, Apapaya	Avodiré
Apitong	Yang
Apopo	Dibetou
Aprono	Mansonia
Apru, Apuro	Kotibé
Arere	Obeche
Arzagi	Yew
Asamela	Afrormosia
Asna, Asne	Indian laurel
Aspe, Aspen	Poplar
Assacu	Hura
Assang-assie, Assie	Sipo
Assi, Assie	Sapele
Assore	Kosipo
Atom Assie	Kosipo
Avati	Courbaril
Awari	Koto
Awiemfa samina	Iatandza
Awong	Wengé
Axim	African mahogany
Ayab	Moabi
Ayan	Doussié
Ayan	Movingui
Ayin, Ayinre	Afrormosia
Ayous	Obeche
Azodau	Doussié
Azobe	Bongossi
Badi	Bilinga
Bagi	Limba
Bahia	Abura
Bahia rosewood	Brazilian rosewood
Bajee, Bajii	Framiré
Baka	Kotibé
Baku	Makoré
Balaké	Kotibé
Bangui	Kambala
Bark	Framiré
Barkeloth tree	Antiaris (Bonkonko)
Barre	Movingui
Barwood	African Padauk
Bassi	Framiré
Basswood	American whitewood

	Standard name
Bataan	Red meranti
Batuan	Dao
Baywood	American mahogany
B'boti	Framiré
Benge, Bengi	Mutenye
Benin mahogany	African mahogany
Bété	Mansonia
Bhera	East Indian satinwood
Bibitu	Sapele
Bibolo	Dibetou
Bili	Limba
Bilsted	American red gum
Biri	Dibetou
Bisselon, Bissilongo	African mahogany
Biti	Rosewood
Black Afara	Framiré
Black hickory nut	American walnut
Boana	Agba
Bobwe	Sapele
Bofo ovale	Koto
Bohalala	Afrormosia
Bois de rose	Bahia rosewood
Bokongo	Bubinga
Bokongo	Dibetou
Bokonge	Wengé
Bokuku	Agba
Bokungu	Dabema
Bolengu	Doussié
Bolimba	Agba
Bombalu	Dibetou
Bombanga	Doussié
Bombay blackwood	East Indian rosewood
Bona	Framiré
Bonkangu	Bilinga
Bonkonko	Antiaris
Bonsamdua	Ayan, Movingui
Bontue	Koto
Bope-bambale	Niové
Boroua	Mansonia
Bosassa	Bossé
Bosolu	Padauk
Bosassa	Niové
Bossé, Bossi	Guarea

	Standard name
Boti	Framiré
Bouboussou	Sapele
Bouleau blanc	Birch
Bousousson rouge	Kosipo
Bovili	Antiaris (Bonkonko)
Brazilian walnut	Imbuia
Bucheira	Peroba rosa
Burus, Burutu	East Indian satinwood
Buvenga	Bubinga
Cabeuna	Brazilian rosewood
Caixeta	Ipé
Calicedro	Cedrela
Cambogala	Okoumé
Cambore	Brazilian rosewood
Camwood	African Padauk
Carna	American walnut
Canaletto	American walnut
Canary wood	American whitewood
Canela foreta, negra, preta	Louro preto
Canella imbuia	Imbuia
Canuguate	Ipé
Caoba	American mahogany
Carobeira	Ipé
Caryon	Walnut
Castagno, Castano	Chestnut
Cauri	Framiré
Caviuna	Brazilian rosewood
Cay ca-gan	Indian laurel
Cedar, Cedrela, Cedro	American cedar
Cedro cebello	American mahogany
Cerisier	Cherry
Cevitza	Walnut
Chai	White meranti
Chanfuta	Afzelia
Chenchen	Antiaris (Bonkonko)
Chêne	Oak
Chiculte	American mahogany
Choga	Yew
Ciliegio	Cherry
Cimiri	Courbaril
Coapinal	Courbaril
Coeur de hours	Sucupira
Combo Combo	Okoumé

	Standard name
Congowood	Dibetou
Copal, Copalier, Copinol	Courbaril
Corail	Padauk
Corina	Limba
Corla	Sequoia
Corobore	Courbaril
Coromandel	Macassar ebony
Crura	American mahogany
Cucumber tree	American whitewood
Cunculo	Moabi
Dahoma	Dabema
Daku	Moabi
Damar	Meranti
Danta	Kotibé
Debé	Kotibé
Degema mahogany	African mahogany
Dehor	Framiré
Demohi	Dao
Determa	Red Louro
Dhunu	Yew
Diambi	Bossé
Diamuni	Kosipo
Dikala-kala, Dikela	Wengé
Dikase kasa	Iatandza
Dilolo	Sapele
Dilolo fiote	Dibetou
Dimori	Makoré
Dimpampi	Moabi
Diolosso	Antiaris
Distemonanthus	Ayan
Divuiti	Bossé
Djati	Teak
Djave	Moabi
Djongoamba	Iatandza
Dominguila	Dibetou
Duabai	Movingui
Dubimi mahogany	African mahogany
Dumori	Makoré
Eba	Bongossi
Ebanghemwa	Bossé
Ebène jaune, E.verte	Ipé
Edinam	Gedu nohor, Tiama
Edo	Movingui
Edoussié	Doussié, Tiama
Efam	Moabi
Efau-Konkonti	Sipo
Efok	Koto
Egbi	Afrormosia
Egoin	Limba
Ejen	Afrormosia
Ekbale	Limba
Ekhimi, Ekkimi	Dabema
Ekki	Bongossi
Ekop	Niové
Elolom	Abura
Elo uta	Afrormosia
Emri, Emeri	Idigbo (Framiré)
Eng	Yang
Engan	Avodiré
Epicea	Spruce
Eprou	Kotibé
Erable	Maple
Eravadi kalaruk	Rosewood
Erun	Tali
Esaka	Kosipo
Esaki	Tiama
Essec	Iatandza
Essingang	Bubinga
Estoraque	American sweet gum
Eucalitto	Eucalyptus
Eyan	Dibetou
Eyen	Movingui
Faggio	Beech
False Iroko	Bonkonko
Farayen	Limba
Fela	Framiré
Foltha larga	Imbuia
Fou	Bonkonko
Frake, Frameri, Framo	Limba
Framire	Idigbo
Frassino	Ash
Freijo	American cordia
Frene	Ash
Gaboon, Gabun	Okoumé
Gedu lohor, G.noha, G.nohor	Tiama
Gia thi	Teak

	Standard name
'Gold teak'	Afrormosia
Gongo moitomo	Macassar ebony
Goma colorado	American sweet gum
Grand bassam	African mahogany
Greenheart	Ipé
Grogoli	Anegre
Guapinol	Courbaril
Guarea	Bossé
Guayacan	Ipé
Gurjun	Yang
Habas	Dao
Hadri	Indian laurel
Halda	East Indian satinwood
Hamrak	Dao
Haoul	Chestnut
Hatna	Indian laurel
Hazel pine	American sweet gum
Hêtre	Beech
Hickory poplar	American whitewood
Holda	Indian laurel
Hudoke	Sucupira
Hurgalu	East Indian satinwood
Hwamu	Chestnut
Iataiba	Courbaril
Iba	Yew
Ibira romi	Peroba rosa
Idigbo	Framiré
If	Yew
Ikwapobo	Kosipo
Ing	Yang
Intuele, Intule	Kambala
Ipaki	Tiama
Ireme	Framiré
Iroko, Iroco	Kambala
Ischingesha	Iatandza
Itaiba	Courbaril
Izingana	Zebrano
Jati	Teak
Jatoba	Courbaril
Jenni	Courbaril
Julchihout	Courbaril
Junero	Brazilian rosewood
Jutahi, Jutay	Courbaril

	Standard name
Ka-bari	Dabema
Kaku	Bongossi
Kali	Anegré
Kalulu	Bonkonko
Kalungi	Tiama
Kamaj	Moabi
Kamashi	Niové
Kamassi	Knysna boxwood
Kambi	Moabi
Kanawang	Meranti
Kà tema	Kambala
Kaya garu	Ramin
Kedire	Teak
Kefe	Koto
Kembal	Teak
Kendra	Courbaril
Kevazingo	Bubinga
Keruing	Yang
Kiboto	Wenge
Kiombe	Bubinga
Kion	Koto
Kirundu	Bonkonko
Kisésé	Padauk
Kitola	Tchitola
Klatie	Kosipo
Koan	Meranti
Koili	Dao
Kojoe itam	Macassar ebony
Koki phonom	Meranti
Kokango	Framiré
Koko	Siris
Kokongo	Doussié
Kol	Walnut
Kokrodua	Afrormosia
Kongo	Bubinga
Korina	Limba
Kosi kosi	Sipo
Kotibé	Danta
Kouan	Mutenye
Koul	Mansonia
Koyagei	Limba
Krasse	Bossé
Krot	Walnut

	Standard name
Kungulu	Moabi
Kusiaba, Kusiabo, Kusia	Bilinga
Kwanari	Courbaril
Kyenkyen	Bonkonko
Kyere	Koto
Kyonix	American sweet gum
Kyun	Teak
Lanutan-bagio	Ramin
Lapacho	Ipé
Laup	Dao
Legno corallo	Padauk
Legno rosa	Pau rosa
Lianu	Bubinga
Libayo	Tiama
Libenge, Libengi	Mutenye
Libuyu	Sapele
Libuyu	Kosipo
Lidia	Framiré
Lifaki	Sapele
Lifaki	Tiama
Lifaki moindu	Dibetou
Lifaki mpembe	Kosipo
Lifaki pembe	Dibetou
Lifow	Avodiré
Lifuco	Kosipo
Liquidambar	American sweet gum
Locust	Courbaril
Log-otsi	Bonkonko
Lokoa popo	Tiama
Lolagbola	Tchitola
Longo	Tiama
Lotue	Sapele
Lovoawood	Dibetou
Luet	Yew
Lumbern	Meranti
Luole	Bubinga
Lupigi	Dao
Lusamba	Avodiré
Macula	Spotted gum
Madera negra	Indian laurel
Mai Sak	Teak
Maitem	Macassar ebony
Majaine	American mahogany
Makaba	Chestnut
Makadany	Dao
Makai	Meranti
Makarou	Makoré
Mamakau	Dao
Maranda	Tchitola
Marbre	Courbaril
Maripende	American sweet gum
Mayapis	Red meranti
M'banga	Doussié
M'babou	Makoré
M'babou	Tchitola
M'bel	Padauk
M'benge	Bubinga
M'bengi	Mutenye
M'bero	Dibetou
M'beza	Pau rosa
M'bonda	Niové
M'bosse	Bossé
M'boti	Framiré
M'boun	Niové
Mebrou	Sapele
Mebrou zuiri	Sipo
Melapi	Meranti
Melavis	Ramin
Melèze	Larch
Memenga, Menga-menga	Niové
M'gunda	Kambala
Mibotu	Wengé
Mirim	Sucupira
Missanda	Tali
Mkora	Afzelia
Mnai	Pau rosa
Moboron	Agba
Mogano	American mahogany
Mogoubi	Niové
Mohole	Afrormosia
Mojondi	Macassar ebony
Mokolé	Afrormosia
Mologotoe	Macassar ebony
Molondou	Kambala
Momboyo	Sipo
Monga	Bubinga

	Standard name
Monkonge	Wengé
M'pele	Agba
Moreira	Kambala
Moutchibanaie	Dibetou
Movingui	Ayan
Mucarane	Pau rosa
Muenge	Padauk
Mufula	Kambala
Mukali	Anegré
Mukama	Dibetou
Mukangu	Anegré
Mukonia	Abura
Mukumi, Mukushi	Tiama
Mukusi, Mukusu	Taima
Mulatchine	Pau rosa
Mulimba	Limba
Mumangala	Doussié
Muna	Anegré
Mundambi	Wengé
Murada	Indian laurel
Musase	Iatandza
Museka	Agba
Musharagi	East African olive
Musongo	Iatandza
Mutene	Mutenye
Mutigbanaye	Bossé
Mutsanya	Kotibé
Mutsekamambole	Agba
Mut(t)i	Indian laurel
Muvenghi	Movingui
Muyembe	Moabi
Muyovou	Taima
M'vovo	Sapele
M'vule	Kambala
Nazareno	Courbaril
N'dola	African mahogany
Neang peak	Indian laurel
Nemesu	Meranti
N'gollon	African mahogany
N'gondou	Wengé
N'gula	Padauk
N'gulumaza	Bilinga
Nhire	Pau rosa
'Nigerian satinwood'	Movingui
Niabi	Mobai
Njame	Dao
Noce	Walnut
Noce africano	Dibetou
Noce mayombe	Limba
Noce tanganika	Anegré
Nogal	Walnut
Noibwood	Ipé
Noyer	Walnut
Nson-so	Wengé
N'tola	Agba
N'towo	Abura
Nungu	Moabi
N'vero	Dibetou
Nyankom	Niangon
Nzali	Padauk
Obasuluk	Meranti
Obeche	Abachi
Obobo-nofwa	Guarea (Bossé)
Odo	Doussié
Odo	Mansonia
Odum	Kambala
Afram	Limba
Ofun	Mansonia
Ogbon-eli	Mutenye
Ogiovu	Bonkonko
Ogové	Niangon
Ogueminya	Movingui
Ogwango	African mahogany
Okeang	Sipo
Oko	Moabi
Okoume	Gaboon
Okpe	Movingui
Ole	Afrormosia
Olivo	Olive wood
Olmo	Elm
Omo	Cordia
Ombolo M'bolo	Dibetou
Omu	Kosipo
Ongo ayem	Iatandza
Onidijo	Framiré
Opapea	Anegré

	Standard name
Opepe	Bilinga
Oporipo	Koto
Orere	Moabi
Ori	Anegré
Ormeau, Orme champêtre	Elm
Oro	Bonkonko
Oroko	Kambala
Oropa	Niové
Orura	American mahogany
Osan	Anegré
Osun	Padauk
Otutu	Kotibé
Ovang	Bubinga
Ovoé, Ovové	Kotibé
Ozocote	American sweet gum
Ozonga	Okoumé
Pahi	Teak
Paldao	Dao
Palo colorado	Sequoia
Pao hua	Chestnut
Papao	Doussié
Pau cravo	Bahia rosewood
Pau d'arco	Ipé
Pearwood	Moabi
Penkwa	Dibetou
Penkwa	Sapele
Peroba dos campos	White Peroba
Peterebt	Louro preto
Pha-yom	Meranti
'Pink ivory wood'	Pau rosa
Pioppo	Poplar
Pohouro	Koto
Poirier d'Afrique	Moabi
Popple	American whitewood
Poroposo	Koto
Porsuk ag	Yew
Possentrie	Hura
Potodrom	Tali
Proboko	Antiaris (Bonkonko)
Pruno	Mansonia
Pterygota	Koto
Pue	Agba
Puget sound pine	Oregon pine
Quercia	Oak
Quizarra	Louro preto
Ramin telur	Ramin
Reang phak	Indian laurel
Redbark	Afrormosia
Red peroba	Peroba rosa
Redwood	Sequoia
Rokko	Kambala
Sabica	American mahogany
Saborana	Brazilian rosewood
Sagon	Teak
Saia, Sain	Indian laurel
Sak	Teak
Sali	East Indian satinwood
Samarie-japo	Cedrela
Samba	Obeche
Samfona	Anegré
Sapin	Fir
Sapoton	American mahogany
Sapupira preta	Sucupira
'Satin walnut'	American sweet gum
Sebipira	Sucupira
Sekundi	African mahogany
Semarang	Teak
Semli	Kambala
Sengel	East Indian satinwood
Sengkuane	Dao
Senhungo	Kotibé
Shingle wood	Framiré
Shisham	Rosewood
Sibo	Bilinga
Sida	Dibetou
Sifou-sifou	Iatandza
Sifu	Doussié
Simme	Kambala
Simi	Courbaril
Singa	Dabema
Siris	Kok(k)o
Songo	Avodiré
Sonokling	Rosewood
Sonosoengoe	Rosewood
Stanthorpe yellow-jacket	Eucalyptus
Subaha	Abura

	Standard name
Sungangona	Pau rosa
Sungula	Doussié
Sussu-menga	Niové
Tacoradi	African mahogany
Tadi	Teak
Tallowwood	Blue gum
Tali	Missanda
Tanga tanga, Tango	Iatandza
Tanguile	Red meranti
Tasso	Yew
Tataboe	Sucupira
Tegina	Teak
Teio	Yew
Temamire	Dibetou
Terminalia	Framiré
Thekku	Teak
Thona	Yew
Timbi	Sipo
Timbi	Tiama
Timbi	Sapele
Tindalo	Doussié
Tinyu	Yew
Tola, Tola blanc	Agba
Tola chinfuta, Tola mafuta	Tchitola
Toum	Dabema
Toumbohiro noir	Kambala
Tremble	Poplar
Tsangu	Bonkonko
Tsanya	Kotibé
Tsibudimba	Tchitola
Tsikalakala	Wengé
Tshimaye	Tiama
Tshimaje noir, T.rouge	Sipo
Tsuga de patton	Hemlock
Tuba	Tchitola
Tubini	Dibetou
Tulipwood, tulip tree	Amer.whitewood
Tungi	Mutenye
Ubelu	Agba
Ubilesan	Sapele
Ubiri	Framiré
Undianunu	African mahogany
Urodo	Mansonia
Utilé	Sipo
Uvala	Doussié
Vavona	Sequoia
Vermilion wood	Andaman Padauk
Voukov	Abura
Vovo	Sipo
Vummarary	East Indian satinwood
Wahala	Afrormosia
Waka	Bubinga
Walola	Afrormosia
Walola	Bubinga
Wamba	Agba
Wane	Red Louro
Wanga	Niové
Wansenwa	Avodiré
Waré	Koto
Washiba	Ipé
Wawa	Obeche
Wawampe	Koto
We-we	Brazilian rosewood
'White Afara'	Limba
Wombolu	Dibetou
Xen	Meranti
Yaga-bito	American sweet gum
Yalam	Cedrela
Yali	Yew
Yang-gulk	Walnut
Yatandza	Iatandza
Yellow poplar	American whitewood
Yembe	Moabi
Ysipo-oby	Bahia rosewood
Yulu	American mahogany
Zambesi redwood	'Rhodesian teak'
Zante wood	East Indian satinwood
Zapatero	Maracaibo boxwood
Zingana	Zebrano
Zopilote	American mahogany
Zougou-ban	Tiama
Zwarte kappes	Sucupira

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